

**PROMOTING ENHANCED MOTOR PLANNING IN PROSTHESIS  
USERS VIA MATCHED LIMB IMITATION**

A Dissertation  
Presented to  
The Academic Faculty

by

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In Partial Fulfillment  
of the Requirements for the Degree  
Doctorate in the  
School of Applied Physiology

Georgia Institute of Technology  
May 2014

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# **PROMOTING ENHANCED MOTOR PLANNING IN PROSTHESIS USERS VIA MATCHED LIMB IMITATION**

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*Dedicated to my wife, Katharine, for eternal love, unending support, sturdy Quin,  
and for saying “Apply.”*

*“From here to the eyes and the ears of the 'Verse, that's my motto.  
Or at least it might be, if I start having a motto.”  
-Mr. Universe*

## ACKNOWLEDGEMENTS

I would like to thank my:

Wife again, because no number of thanks will ever suffice.

Son, Quin, for playing Dadda Monkey with me.

Mom, Denise, for nights of stargazing and hypothesizing.

Dad, Bill, for teaching me to think critically.

Sister, Annie, for Rocket Power.

Mother-in-law, Ann, for being perpetually excited about my research.

Father-in-law, Lou, for late night talks about the Higgs boson and beyond.

Parents-in-law, Ann and Lou, for generous, thoughtful, and loving care of Quin.

Research advisor, Dr. Wheaton, for unwavering support in science, and above all, in life.

Academic advisor, Dr. Nichols, for guiding me from “engineer” to “scientist/engineer.”

PhD committee, for considerate feedback and helpful suggestions.

Unofficial 6<sup>th</sup> committee member, Dr. Mizelle, for patience, constructive criticism, and beer recommendations.

Labmates, Nik and Rachel, for research ideas, moral support, and countless EEG preps.

Student army: Mike, Sheryl, Scott, Rebecca, Delisa, Regan, Briana, Sarah, and Ashley.

Subjects with amputations, for providing the grounding motivation for this dissertation.

First advisor, Mr. Lynn, for introducing me to science, engineering, technology, Science Olympiad, and mountain biking.

Childhood dogs, for eating my Ninja Turtles, thus forcing me to rebuild them as cyborgs.

LEGOs, popsicle sticks, and glue gun, for giving me a way to rebuild my Ninja Turtles.

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## SUMMARY

As of 2005, there were over 1.5 million amputees living in the United States, more than 548,000 of them with upper extremity involvement. The total number of amputees is projected to rise to at least 2.2 million by 2020. Unfortunately, full functional use of upper extremity prosthetic devices is low. Knowledge gained regarding the cortical systems active in amputees performing motor tasks may reveal atypical motor control strategies that contribute to these issues. Substantial evidence demonstrates a strong dependence on left parietofrontal cortical areas to successfully plan and execute tool-use movements and pantomimes. It was previously unclear how this network functioned in users of prostheses. The hypothesis of this dissertation is that in order to optimally engage the typical parietofrontal network during action imitation with a prosthetic device, the action being imitated should be performed by a matching prosthesis. Also, that greater engagement of the parietofrontal network will result in increased ability to perform tool-use movements.

First, this dissertation showed that when imitating motor tasks performed by intact actors, prosthesis users exhibit lower engagement of the parietofrontal action encoding system. This network is crucial for motor adaptation. Left parietofrontal engagement was only observed when prosthesis users imitated matched limb prosthesis demonstrations, which suggests that matched limb imitation may be optimal to establish motor representations. Next, intact subjects donned a fictive amputee model system (FAMS) to simulate the limb movement that transradial amputees experience. Matched limb imitation in FAMS users yielded better movement technique compared to mismatched

imitation. Finally, the longitudinal effects of a matched limb training paradigm on the cortical action encoding activity and motor behavior in FAMS users were investigated. Matched limb imitation subjects showed greater engagement of the parietofrontal network and better movement technique compared to those trained with mismatched limb.

This dissertation has clinical relevance as it supports the notion that matched limb imitation could play an important role in the performance of motor tasks using a prosthetic device. These findings could be used to inform the development of improved rehabilitation protocols that may lead to greater functional adaptation of prosthetic devices into the lives of amputees.

# **CHAPTER 1**

## **INTRODUCTION**

### **Problem Definition**

As of 2005, there were over 1.5 million amputees living in the United States, with more than 548,000 individuals having some level of upper extremity involvement. The total number of amputees is projected to rise to at least 2.2 million by 2020 (Ziegler-Graham et al. 2008). In order to preserve their independence and quality of life, amputees learn how to successfully perform daily living tasks with their artificial limb. It has been demonstrated that functional adaptation to prosthetic devices is low, with up to 33% of upper extremity amputees abandoning their prostheses, in large part due to a perceived lack of usefulness in daily life. Further, 75% of amputees view their artificial limbs as functional aesthetic devices whose principal purpose is to restore symmetry to their appearance (Datta et al. 2004; Biddiss and Chau 2007a; Biddiss and Chau 2007b). Knowledge gained regarding the cortical systems active in amputees while planning and performing motor tasks may reveal atypical motor control strategies that contribute to these issues. Deviations from normal control strategies may influence the degree to which a patient successfully incorporates their device into activities of daily life (ADLs) (Cohen et al. 1991; Rossini et al. 2011).

For subjects with intact upper extremities, substantial evidence demonstrates a strong dependence on left parietofrontal cortical areas to successfully plan and execute tool-use movements and pantomimes (Hermsdorfer et al. 2007). These same cortical areas have been described as possessing mirroring qualities in that they are active during

the performance of a motor task and during the observation of the performance of a motor task. This finding merges the neural substrates of action perception and action execution (Cattaneo and Rizzolatti 2009). However, it is controversial as to whether the parietofrontal network is active when observing actions performed by a non-human actor such as a robotic arm (Tai et al. 2004). It has been suggested that in these cases, areas in the parietooccipital network may be responsible for the visuomotor processing of unfamiliar actions outside of one's own motor repertoire (Aziz-Zadeh et al. 2012). It remains unclear how the parietofrontal action perception-execution system functions in upper extremity amputees who are learning to use their devices. This is a vital question, as the parietofrontal system has been shown to be important for motor adaptation (Buch et al. 2012); a process that could be important for amputees learning how to use new prosthetic limbs (Bouwsema et al. 2008; Schabowsky et al. 2008; Bouwsema et al. 2010b).

The central hypothesis of this dissertation is that in order to optimally engage the typical parietofrontal network during action imitation with a prosthetic device, the action being imitated should be performed by a matching prosthetic limb. When training with a matched prosthetic limb, we predict that greater engagement of the typical parietofrontal network will occur, along with increased ability to successfully plan and execute tool-use movements. This hypothesis will be investigated in amputees using their prosthetic device and in intact subjects using a fictive amputee model system (FAMS); which consists of a specially adapted prosthetic device that fits over the intact limb.

An alternative to the central hypothesis is that observation and imitation of both a matched and a mismatched prosthetic limb equivalently engages the parietofrontal

network during action imitation with a prosthetic device. This result would suggest that engagement of the action observation network is end-effector independent in prosthesis users. An additional alternative hypothesis is that prosthesis users demonstrate equivalent ability to perform action imitation movement despite differentially engaging the parietofrontal versus parietooccipital action encoding networks. This result would suggest that prosthesis users perform motor task imitation similarly while relying on the engagement of different cortical action encoding mechanisms.

The engagement of the cortical action encoding networks will be quantified by neural recording using electroencephalography (EEG) in both amputees and FAMS users as they perform tool-use activities with their respective devices. Behavioral performance will be measured by electrogoniometry (ELGON). The goal of this dissertation is to use basic neuroscience findings to inform the development of improved rehabilitation protocols that lead to greater functional adaptation of upper extremity prosthetic devices into the lives of amputees.

## **Research Aims**

### **Specific Aim #1**

#### Question

In amputees, is parietofrontal action encoding during task imitation influenced by the type of arm imitated?

#### Aim

To investigate the parietofrontal activation differences in amputees using prostheses during imitation of movement of intact limbs versus prosthesis users.

### Hypothesis

In amputees, imitation of other prosthesis users will show greater activation of typical parietofrontal action encoding regions compared to imitation of intact limbs, which will show greater activation of parietooccipital regions.

### Approach

Using EEG, cortical activations were evaluated during movement planning and execution in amputee prosthesis users to determine if parietofrontal areas are engaged to a greater extent when imitating actions performed by a prosthesis that matched their own.

### **Specific Aim #2**

#### Question

In intact FAMS users, is motor behavior during task imitation influenced by the type of arm imitated?

#### Aim

To investigate the motor behavior differences in intact FAMS users during imitation of intact versus prosthesis user movements.

#### Hypothesis

Intact FAMS users will elicit less joint motion variability when imitating a prosthesis user compared to imitating an intact actor, which will elicit greater variability.

#### Approach

Using ELGON, joint angles were recorded to determine whether intact FAMS users perform motor tasks with greater consistency when imitating actions performed by a limb that matches their own.

### **Specific Aim #3**

#### Question

Can longitudinal parietofrontal network activity and motor performance be influenced during FAMS training with video imitation of another prosthesis user?

#### Aim

To investigate the longitudinal cortical and motor behavior differences in intact FAMS users during training with imitation of intact actor versus prosthesis user movements.

#### Hypothesis

Intact subjects trained using the FAMS via video imitation of another prosthesis user will show more longitudinal engagement of the typical parietofrontal regions and less joint motion variability than their counterparts trained via video imitation of an intact actor.

#### Approach

This aim combines EEG and ELGON in a longitudinal paradigm to investigate if parietofrontal cortical activity and motor behavior in intact FAMS users can be influenced differentially as a function of the type of video observed and imitated during a week-long training regimen.

## **Organization of the Dissertation**

This dissertation is organized into eight chapters and appendices. Chapter 2 introduces the relevant work in cortical action encoding systems that provides the groundwork for the questions addressed in this dissertation. In Chapter 3, the methodologies implemented in this work are introduced and justified. The short term cortical and behavioral effects of matched limb imitation are investigated in persons with amputation, intact subjects, and FAMS users in Chapters 4, 5, and 6 (Specific Aims #1 and #2). Chapter 7 examines the longitudinal cortical and behavioral effects of matched limb imitation in FAMS users (Specific Aim #3). Within these chapters, the study rationale is reiterated, and methodology, results, and discussion are presented. Finally, Chapter 8 provides a summary of the dissertation findings along with discussion of future work.



## **CHAPTER 2**

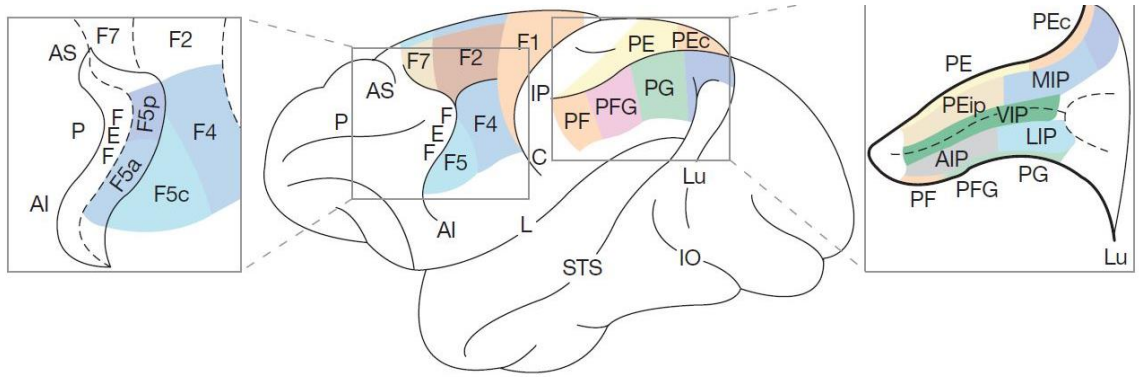
### **BACKGROUND**

#### **Neuroanatomy of Action-encoding Networks**

This dissertation involves in-depth discussion of two primary cortical action encoding networks: parietofrontal and parietooccipital. Both of these networks have been implicated as playing important roles in action observation and action execution, and as such, are critical in interpreting the presented results. Much of the discussion will focus on the functionality of these networks in the context of action imitation in users of prosthetic devices, and the potential influence that this cortical activity has on the corresponding motor behavior. The aim of this section is to lay the neuroanatomical groundwork for this discussion by explicitly detailing the important cortical structures involved in the parietofrontal and parietooccipital networks.

#### **Parietofrontal Network**

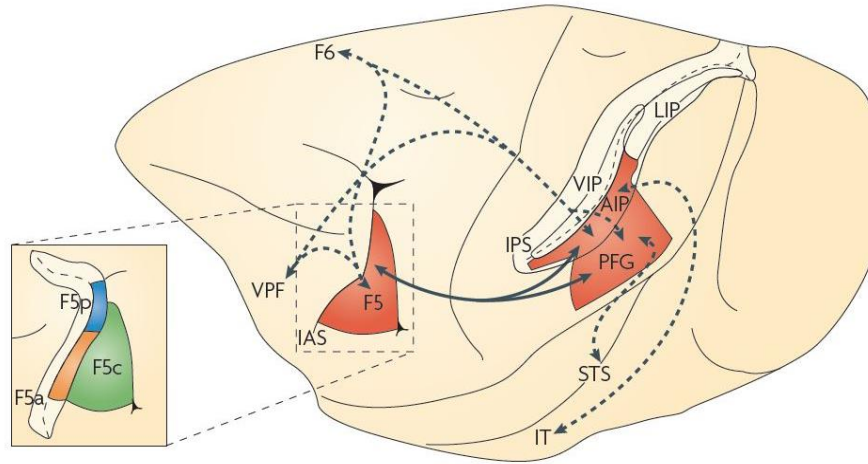
The parietofrontal network (Figure 2.1 (Cattaneo and Rizzolatti 2009), was initially identified and characterized in the macaque monkey model (di Pellegrino et al. 1992).



**Figure 2.1:** A map of the macaque cortex with focus pointed to areas in the parietal (PE, PEc, PF, PFG, PG) and frontal regions (F7, F2, F1, F4, F5) (adapted from Rizzolatti et al. 2009 with permission from publisher). AIP = anterior intraparietal sulcus, LIP = lateral intraparietal sulcus, MIP = medial intraparietal sulcus, VIP = ventral intraparietal area.

In a landmark set of electrophysiological studies by Rizzolatti et al., a subset of cortical neurons were found to be active in the ventral premotor cortex both during the execution of an action and the observation of that same action performed by another agent, and were thus termed “mirror neurons” (di Pellegrino et al. 1992; Gallese et al. 1996; Rizzolatti et al. 1996). Later, additional areas in the macaque parietal cortex were also found to exhibit similar mirroring properties. A study by Fogassi et al. revealed neuronal activity in the inferior parietal lobule (IPL) corresponding to both the performance of a grasping motor task as well as the observation of that same task performed by the experimenter (Fogassi et al. 2005). Within the IPL, it has been suggested that activity specific to the anterior intraparietal area (AIP) and area PFG may assist the observer in understanding goal-directed motor actions of the observed from their own internal perspective (Fogassi et al. 2005; Rozzi et al. 2008; Rizzolatti et al. 2009). The connectivity between the parietal and frontal areas has also been studied closely in the macaque (Figure 2.2 (Rizzolatti and Sinigaglia 2010)). A histological study by Rozzi et

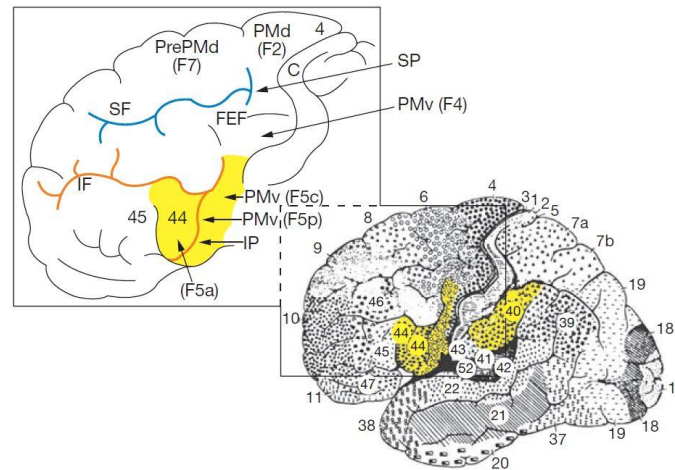
al. used fluorescent tracers to reveal significant cortical projections between areas in the IPL (PFG, AIP) and F5 (F5c, F5a) (Rozzi et al. 2006).



**Figure 2.2:** A map of the macaque cortex with focus pointed to connectivity between parietal (PFG, AIP) and frontal regions (F5) implicated in parietofrontal mirror network (adapted from Rizzolatti and Sinigaglia 2010 with permission from publisher). AIP = anterior intraparietal area.

The existence of a parietofrontal network in humans (Figure 2.3 (Rizzolatti et al. 2009)) for encoding of seen actions has been supported by studies using functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS), EEG and magnetoencephalography (MEG). In an fMRI experiment involving action observation in humans, Buccino et al. revealed activations in areas of the frontal and parietal cortices typically recruited during action execution (Buccino et al. 2001). Specifically, the frontal areas included: inferior precentral gyrus, inferior frontal gyrus (IFG), dorsal premotor cortex (PMd) and ventral premotor cortex (PMv), and the parietal areas included: inferior parietal lobule (IPL), intraparietal sulcus, and super parietal lobule. The authors proposed

that in the context of motor tasks involving objects, frontal areas facilitated the mapping of observed action onto their own motor repertoires, while the parietal areas are engaged to access stored representations of the observed object (Buccino et al. 2001; Rizzolatti and Craighero 2004; Fabbri-Destro and Rizzolatti 2008; Rizzolatti et al. 2009; Rizzolatti and Sinigaglia 2010).



**Figure 2.3:** The parietofrontal network in humans showing cytoarchitectonic subdivisions in the frontal (Brodmann area 44) and parietal regions (Brodmann area 40) (adapted from Rizzolatti et al. 2009 with permission from publisher). PMv = ventral premotor cortex, IP = inferior precentral sulcus.

Further, similar parietofrontal networks have been implicated in motor execution. An EEG study by Wheaton et al. showed corticocortical coherence between parietal and premotor regions during the performance of both tool use and communicative hand gestures (Wheaton et al. 2005a). The results suggested that cortical activity in these two areas was coupled and played a role in the preparation and execution of praxis movements. More recently, Porro et al. used structural magnetic resonance imaging and

white matter tractography to establish the anatomical connectivity of the parietal and frontal regions during the observation of reaching and grasping actions (Molinari et al. 2013). Together, these results strongly support the notion of a parietofrontal network in humans associated with the observation, planning, and execution of upper extremity motor tasks.

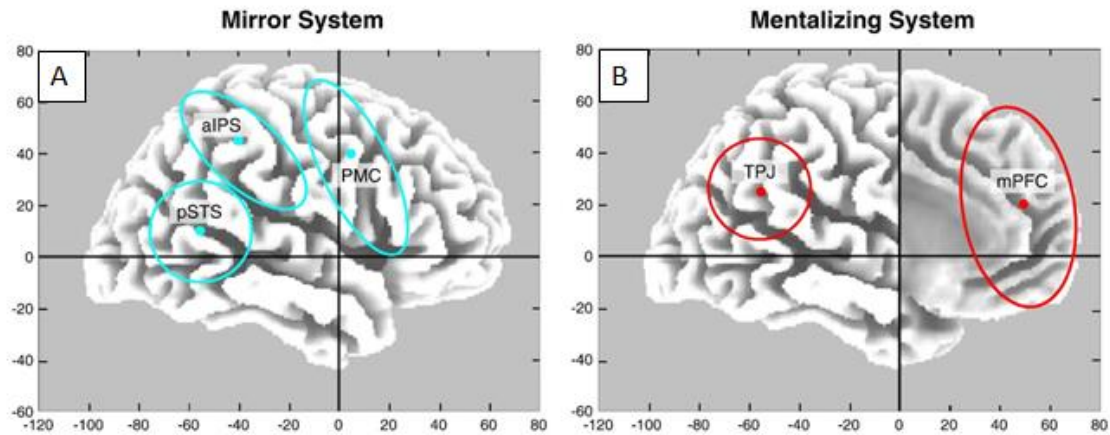
However, some have argued against the notion of a parietofrontal mirroring mechanism in humans for a variety of reasons. First, as mirror properties were initially described in individual neurons in the macaque model (di Pellegrino et al. 1992), some have shown reluctance in ascribing those same attributes to whole brain regions as identified in human brain imaging studies (Rizzolatti and Sinigaglia 2010). Further, it has also been demonstrated that only a small fraction of neurons in the macaque homologue areas actually possess these mirroring qualities (Rizzolatti and Sinigaglia 2010).

### **Parietooccipital Network**

The parietooccipital network, or “mentalizing system” as it is often referred to, relies on the theory of mind, or the ability to understand the goals of another agent as if they were our own (Buccino et al. 2004a; Van Overwalle and Baetens 2009; Spunt et al. 2011). The theory of mind is a quality which is attributed primarily to humans, and thus, has been less validated in the macaque model (Amodio and Frith 2006). However, recent work has begun to explore this quality in macaques. Several studies have demonstrated that area V6A in the macaque parietooccipital cortex exhibits visuomotor properties related to the orientation and direction of hand grasp during object manipulation (Galletti et al. 1997; Fattori et al. 2004; Fattori et al. 2005). Further, recent studies by Fattori et al. and Galletti et al. revealed significant connectivity of area V6A to areas of the anterior

intraparietal sulcus, dorsal premotor cortex, and primary visual cortex (Galletti et al. 2003; Gamberini et al. 2009). Together, these results suggest a neuroanatomical view of how these parietal and occipital areas could function together as part of the motor system for the visuomotor transformations required to understand the actions of others. Finally, it has been suggested that area V6A in the macaque may serve as a homologue for the superior parietal lobule, a candidate cortical structure underlying the proposed mentalizing system in humans (Galletti et al. 2003). More recently, an fMRI study by Mars et al. showed that the middle part of the macaque superior temporal cortex exhibits a connectivity pattern with other visuomotor areas in a similar fashion as the temporoparietal junction in humans; thus suggesting another homologue (Mars et al. 2013).

In addition to the superior parietal lobule and temporoparietal junction, the medial prefrontal cortex has been cited by numerous brain imaging studies as belonging to the parietooccipital network (Figure 2.4 (Van Overwalle and Baetens 2009)) in human (Van Overwalle and Baetens 2009).



**Figure 2.4:** Areas in the human motor cortex associated with the parietofrontal (A) and parietooccipital (B) networks (adapted from Van Overwalle and Baetens 2009 with permission from the publisher). PMC = premotor cortex, aIPS = anterior intraparietal sulcus, pSTS = posterior superior temporal sulcus, TPJ = temporoparietal junction, mPFC = medial prefrontal cortex.

A review report detailed the role of the superior parietal lobule in processing visuospatial imagery and more specifically, in the operation of converting another agent's perspective into their own first-person perspective (Cavanna and Trimble 2006). The authors presented evidence that this region is crucial in the production of self-centered imagery strategies and thus, may be relevant to act of motor imitation. Recent work in developmental psychology has also implicated the temporoparietal junction in the processing and understanding of others' thoughts, goals, and intentions; a key component of the theory of mind. Finally, Van der Cruyssen et al. showed in an EEG study that the medial prefrontal cortex and temporoparietal junction are active early in the process of inferring the behavior of others (Van der Cruyssen et al. 2009).

Two recent fMRI studies have revealed unique functional connectivity of these parietooccipital regions in a variety of contexts. Lombardo et al. demonstrated common

activation of this network during tasks involving mentalizing the self and mentalizing an external agent (Lombardo et al. 2010). The concept put forth by this work was that the mentalizing system is based on a foundation of shared neural representations of the intentions of both the self and external agents. Further parsing the functional connectivity within this network, Atique et al. used fMRI to establish subtle differences in network activity based on the nature of the mentalizing task (Atique et al. 2011). For example, activity in the temporoparietal junction was located more anteriorly for emotional mentalizing and posteriorly for intentional mentalizing. Additionally, during the emotional mentalizing task, functional connectivity was stronger with the medial prefrontal cortex than compared to the intentional mentalizing task. Together, these results strongly support the notion of a parietooccipital network in humans associated with the observation and understanding of other's intentions and behaviors, and in the visuomotor conversion of an external agent's perspective into that of the self.

### **Function of Action-encoding Networks**

Previous studies document that specific areas within the premotor, motor, and parietal cortices are activated when planning, executing and observing cognitive motor control tasks (Cattaneo and Rizzolatti 2009). This network of parietofrontal areas may provide a mechanism by which we can understand, learn, and imitate the actions of others from our own perspective (Rizzolatti and Sinigaglia 2010). The capacity of the parietofrontal network to activate the motor-related areas in the observer is seen in the concept of motor resonance. Motor resonance is defined as when the observation of an action drives an internal replication of that action in the motor system of the observer in a



somatotopic manner (Buccino et al. 2001). This resonance has been shown to excite corticospinal pathways and task-specific muscles during action observation (Strafella and Paus 2000; Funase et al. 2007; van Elk et al. 2011).

According to the ideomotor principle, representations of actions are stored in the form of their effects (Hommel et al. 2001). A bidirectional connection between an action and its effects is established through the association of one's own motor repertoires with the observed effects of the action (Wohlschläger et al. 2003; Hommel 2009). Recent work shows that the parietofrontal network observation effects may be weakened when an individual witnesses a human movement performed by a virtual robotic actor with human-like kinematics. The sensorimotor areas were significantly deactivated when subjects observed a human executing action that was robot-like (Tai et al. 2004; Shimada 2010). This result suggests that the parietofrontal network may be preferentially engaged by limb movements that are similar in appearance and kinematic capabilities to that of the viewer. However, recent studies challenge this account (Rochat et al. 2010).

Evidence also shows sensitivity of the parietofrontal network based on whether the observed action is possible for the observer to perform. It has been shown that observing non-conspecific actions that are not possible in humans activates bilateral visual responses instead of parietofrontal action encoding areas (Buccino et al. 2004b). Similar bilateral and right hemispheric temporoparietal activations have been associated with a mentalizing system, which can be active when actions are observed that have no motor template in the observer (Van Overwalle and Baetens 2009). The mentalizing system may be engaged in visual understanding of unfamiliar actions, rather than using typical parietofrontal action encoding (Wheatley et al. 2007). These results may suggest a

different encoding mechanism for the observation of actions performed with dissimilar limb types.

This alternative action encoding activity is significant, as substantial evidence has demonstrated a strong dependence on left parietofrontal cortical areas to successfully plan and execute tool-use movements and pantomimes (Hermsdorfer et al. 2007; Tsuda et al. 2009). Therefore, the decreased engagement of the parietofrontal network coupled with the increased engagement of the mentalizing system during action observation and imitation may relate to less optimal motor control strategies in amputees learning to use a prosthetic device. The majority of research regarding action encoding and planning mechanisms has been performed in intact and healthy subjects. The aim of this dissertation is to investigate whether neural activations during planning and execution in prosthesis users vary as a function of the type of limb they see performing an action, and how this affects the ability to develop motor patterns for prostheses.

Prior work using EEG to study imitation of tool-use tasks has revealed differential cortical activity based on the familiarity of the action. Imitation pantomime of familiar actions elicited greater activity in the left parietofrontal cortical regions during movement planning, while imitation of unfamiliar actions elicited greater activity in the right temporoparietal-occipital cortical regions (Mizelle et al. 2011). These results corroborate fMRI findings showing greater right temporoparietal-occipital activation upon planning the pantomime of unfamiliar tool-use actions (Vingerhoets 2008; Quallo et al. 2009; Vingerhoets et al. 2011). Together, these findings suggest that the relative engagement of these two action encoding systems is a function of the level of motor resonance between the subject's movement repertoire and the action to be imitated.

Finally, it should be noted that both parietofrontal mirroring and parietooccipital mentalizing networks are potentially activated during the process of motor action observation and understanding. EEG has been successfully used to propose how these networks can function during the course of understanding action goals (left hemispheric) and action intent (right hemispheric) (Ortigue et al. 2010). Specifically, the general framework contains four sequential steps: 1) an initial bilateral posterior activation corresponding to visual processing, 2) near-exclusive activation of left temporal and parietal areas corresponding to understanding the motor act goal, 3) shift in activity from left hemispheric sources to right temporo-parietal areas corresponding to understanding the intentions of others, and 4) decrease in activation across all brain areas except for an increase in orbito-frontal areas (Ortigue et al. 2010). Thus, while both systems are involved in the process, each is responsible for different aspects. As has been discussed above, the relative engagement of these two systems is largely dependent on the type of stimulus presented and how it relates to each individual subject. This dissertation will demonstrate the behavioral benefits of more optimally activating the parietofrontal network instead of relying on the parietooccipital network. To our knowledge, this dissertation represents the first investigation of tool-use imitation action encoding in upper extremity prosthetic device users.

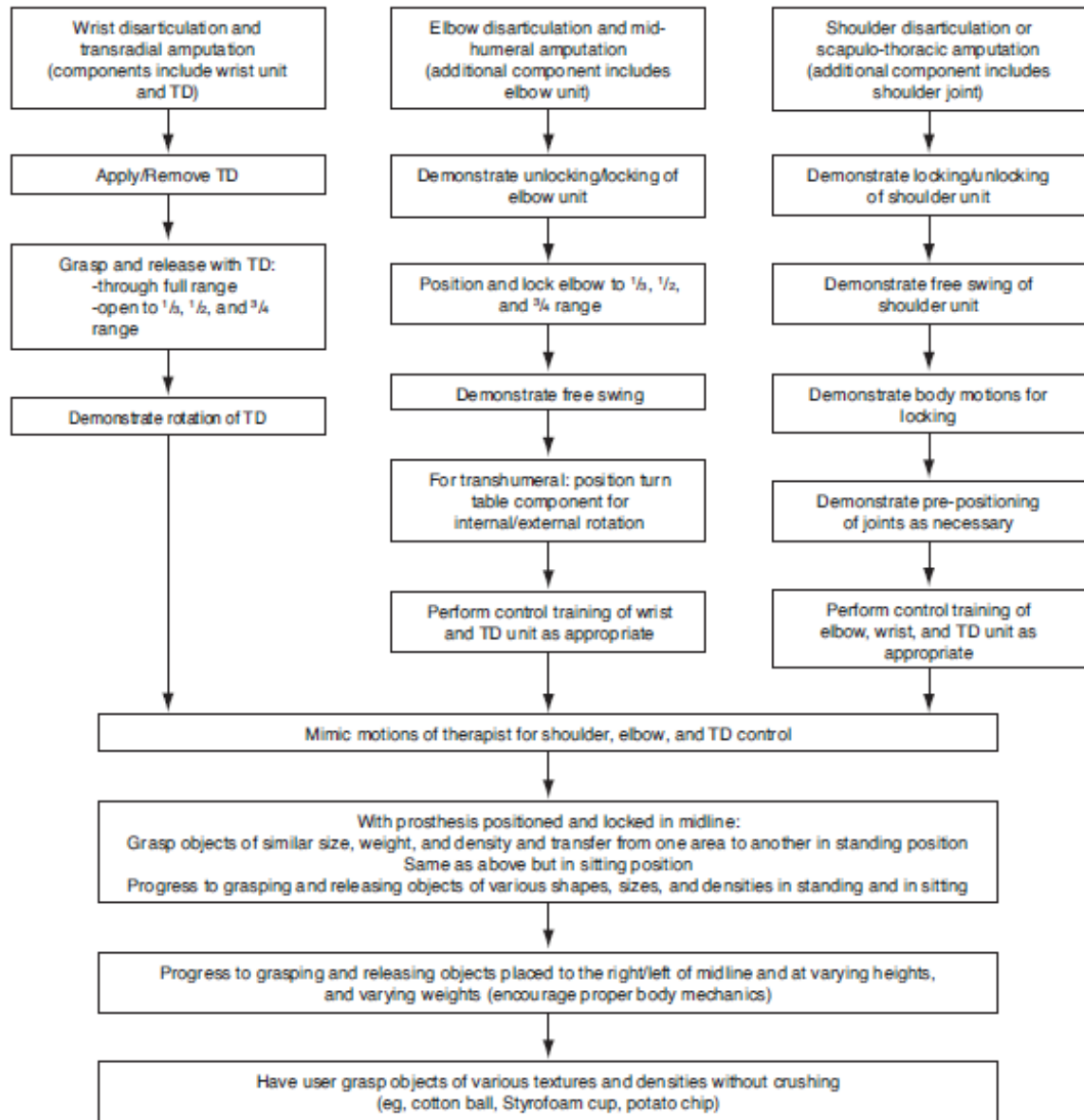
### **Clinical Importance**

It has been established that full functional adaptation of a prosthesis is not common; with 75% of amputees considering their devices to be primarily aesthetic while 33% completely reject the device due to lack of perceived utility (Datta et al. 2004). Amputees cite lack of clear understanding of how to use their devices as well as

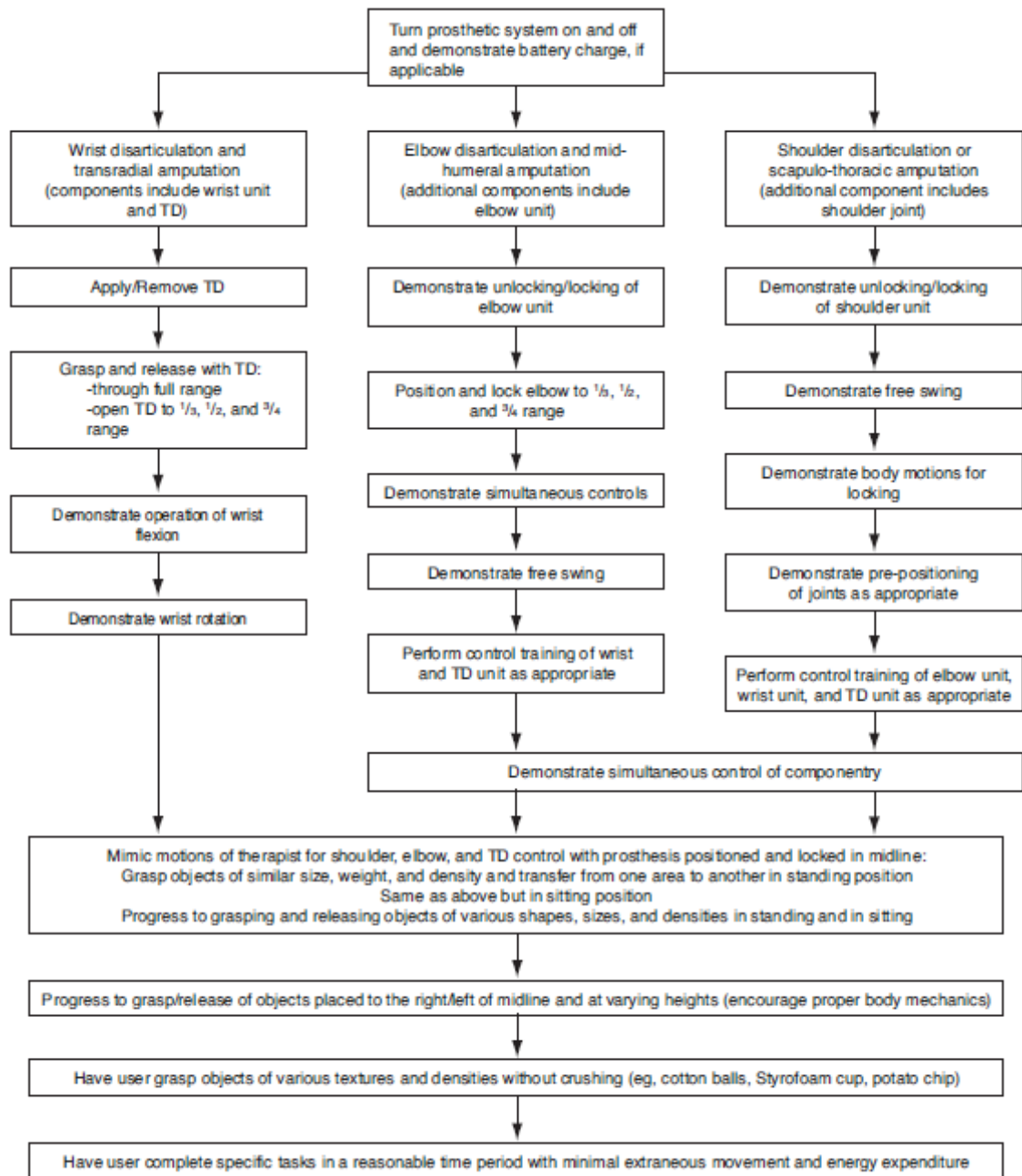
dissatisfaction with the challenge of performing ADLs (Kejlaa 1993; Dudkiewicz et al. 2004). Amputees also encounter challenges in incorporating their prosthesis into tool use tasks due to altered sensory feedback (Ridding and Rothwell 1995; Ridding and Rothwell 1997; Irlbacher et al. 2002; Reilly et al. 2008; Rosen et al. 2009; Gillespie et al. 2010; Stepp and Matsuoka 2010; Rossini et al. 2011) and sense of agency (Ehrsson et al. 2008; Cipriani et al. 2009; Rosen et al. 2009). In addition to these difficulties, amputees report an uncomfortable foreignness when operating their prostheses (Smurr et al. 2008). It has been suggested that these challenges and the corresponding deviations in normal neural control strategies may influence the degree to which a patient successfully incorporates their device into ADLs (Cohen et al. 1991; Rossini et al. 2011).

Customary rehabilitation involves therapist-led training with a focus on: knowledge of the operation and performance of the prosthesis; initiation of controls training; and initiation of training for ADLs (Lake 1997; Smurr et al. 2008). While these fundamental components may be present in many clinical settings, standardized therapeutic methods have not been established (Gaine et al. 1997; Davidson 2002). A notable observation is that occupational therapists administering this prosthesis training are intact and able-bodied individuals themselves. In a recent protocol article by Smurr et al., the authors stated that an integral component of body-powered and myoelectric prosthesis training protocols for persons with all levels of upper extremity amputation is to “mimic motion of therapist for shoulder, elbow, and terminal device control.” Thus, from the onset of their training, amputees are tasked with learning to use their device from an individual with two sound limbs. This results in a scenario similar to that described above where an amputee imitates motor tasks performed by an intact limb.

An important distinction to be made for this dissertation is that the experimental paradigms discussed are not intended to replicate the entire rehabilitative process that a person with upper extremity amputation experiences with their occupational therapist. Instead, the studies are designed to focus on one crucial aspect of this interaction that involves mismatched limb imitation (Smurr et al. 2008). As shown in Figures 8.1 and 8.2, prosthetic rehabilitation is comprised of several rehabilitation activities such as discrete operation of individual joints, limb positioning, grasping, and releasing; most of which are not directly evaluated in the experimental paradigms presented here. Future longitudinal studies could include training sessions that more closely emulate traditional rehabilitation sessions by combining these activities with the additional experimental component of matched limb action observation therapy.



**Figure 2.5:** Controls training for body-powered prostheses for persons with upper extremity amputation at levels of wrist disarticulation/transradial, elbow disarticulation/mid-humeral, and shoulder disarticulation/scapulo-thoracic (adapted from Smurr et al. 2008 with permission from the publisher).



**Figure 2.6:** Controls training for myoelectric prostheses for persons with upper extremity amputation at levels of wrist disarticulation/transradial, elbow disarticulation/mid-humeral, and shoulder disarticulation/scapulo-thoracic (adapted from Smurr et al. 2008 with permission from the publisher).

The central hypothesis of this dissertation is that in order to more optimally engage the typical parietofrontal network during action imitation with a prosthetic device, the action being imitated should be performed by a matching prosthetic limb. In the present state of rehabilitation for amputees learning how to use prostheses, mismatched limb imitation may present a challenge for neural encoding of planning and execution strategies. We posit that learning how to use a prosthesis with a mismatching limb will engage the parietooccipital networks predominantly. We also predict that greater engagement of the typical parietofrontal network will result in increased ability to successfully plan and execute tool-use movements.

Knowledge gained regarding the neural systems activated by prosthesis users while performing motor tasks demonstrated by similar and dissimilar arm types may provide insight into their action planning mechanisms. If additional occipitoparietal activation is required in mismatched limb imitation, this would reveal unique action planning strategies in prosthesis users. These atypical strategies may relate to the challenges experienced by amputees while developing action representations that incorporate a prosthesis.

We propose that amputees engage atypical cortical planning mechanisms as they use their prosthetic device during any therapy featuring this type of limb-mismatched imitation. This activity may be a reflection of the inability of the subject to easily translate the therapist's actions into their own actions. Further comprehension of how this process can be differentially influenced by limb-matched imitation training strategies will inform the future development of novel prosthesis instruction during amputee rehabilitation. The dissertation aims to expand the basic neuroscience understanding of



cognitive motor control in intact subjects and amputees. Specifically, this work will contribute to the understanding of the parietofrontal action planning mechanism while also determining if the engagement of this system has an effect on the motor behavior during task execution with the residual limb and prosthetic device. The creation of improved rehabilitation protocols informed by these basic neuroscience findings may lead to greater functional incorporation of upper extremity prosthetic devices into the lives of amputees.

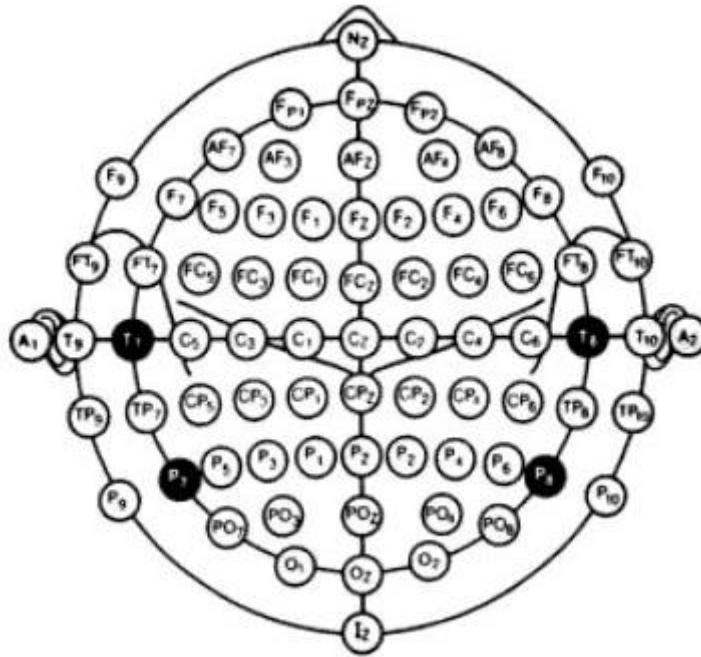
## **CHAPTER 3**

### **EXPERIMENTAL MEASURES**

#### **Electroencephalography (EEG)**

Electroencephalography (EEG) is a non-invasive technique for measuring electrical potentials along the surface of the scalp that are emitted by the cortex. Event-related potentials (ERPs) are time-locked to the onset of a stimulus, which allows for the superposition and averaging of many epochs of data into an aggregate neural signal. The recorded voltages are proposed to originate from the slow and synchronous temporal summation of excitatory post-synaptic extracellular currents (Nunez and Srinivasan 2006). The number of synchronously active pyramidal neurons recorded from by a single EEG electrode has been suggested in the range of tens of thousands to millions (Nunez and Silberstein 2000). Compared to the primary currents propagating within pre-synaptic axons and post-synaptic dendrites, the volume currents that accumulate outside the dendrites are longer lasting. Their amplitudes become additive, resulting in signals large enough to be recorded externally after propagation through the cerebrospinal fluid, skull, and scalp (Nunez and Srinivasan 2006; Cacioppo et al. 2007). Additionally, apical dendrites of pyramidal neurons are largely oriented parallel to one another and perpendicular to the cortical surface, further facilitating the summation of extracellular currents. Contrastingly, pyramidal axons are oriented more randomly, which results in cancellation of fast-acting pre-synaptic extracellular currents (Wyllie 2001; Nunez and Srinivasan 2006).

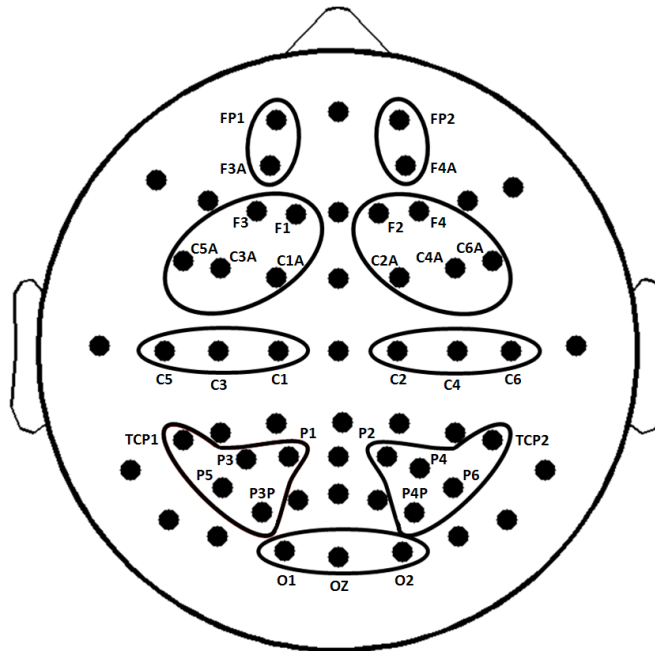
For Specific Aims 1 and 3, subjects were fitted with a 58 channel EEG cap that records scalp potential activity during all movement trials. Electrodes were arranged according to the International 10-20 system (Figure 3.1) (Niedermeyer and Lopes da Silva 2005).



**Figure 3.1:** Standard 64-channel EEG channel layout (International 10-20 system, adapted from Niedermeyer and Lopes da Silva 2005 with permission from publisher).

In these studies, we utilized a cued EEG paradigm to prompt the planning and performance of a tool use pantomime in subjects. These paradigms are often advantageous over self-paced paradigms as they more clearly discern movement related potentials in the planning and execution phases (Jankelowitz and Colebatch 2002). This concept has been demonstrated in prior work using EEG and fMRI to study praxis

movement in healthy subjects (Fridman et al. 2006; Bohlhalter et al. 2009). Finally, EEG electrodes were grouped into regions of interest that were defined in the left and right premotor areas (LPM: F3, F1, C5A, C3A, C1A; RPM: F4, F2, C6A, C4A, C2A), left and right motor areas (LM: C5, C3, C1; RM: C6, C4, C2), left and right parietal areas (LP: TCP1, P5, P3, P1, P3P; RP: TCP2, P6, P4, P2, P4P), and occipital area (OCC: O1, OZ, O2) (Figure 3.2) (Wheaton et al. 2005b; Cusack et al. 2012).



**Figure 3.2:** Regions of interest defined by grouping EEG electrodes.

There are several attributes of EEG that make it the preferable brain imaging technique for this dissertation work. This method allowed for subjects to sit in a comfortable upright position while performing upper extremity motor and tool-use tasks in a naturalistic manner; an advantage over fMRI techniques, which require subjects to

lay prone in a confined space. Additionally, objects with ferromagnetic properties are not permitted within the fMRI scanner, thus excluding the use of prosthetic devices, the FAMS or any related metallic componentry by subjects. This materials restriction also applies to the use of ELGON and would eliminate the ability to simultaneously monitor motor behavior during testing. Compared to fMRI, EEG offers a superior temporal resolution (1 ms versus several minutes, respectively), but inferior spatial resolution (2cm versus 2mm, respectively). Finally, skull thickness differences both within and across subjects have been reported and indicate variability in electrical conductance that may theoretically influence electrical activity recorded on the scalp. However, a recent study demonstrated that this variability was negligible compared to other potential sources of variability in the EEG signal, and thus could be neglected (Hagemann et al. 2008). The other potential sources of intracranial voltage variability between subjects are compensated for during signal processing with baseline correction.

### **Electrogoniometry (ELGON)**

For Specific Aims 2 and 3, two-dimensional motion of the wrist, elbow, and shoulder were collected continuously throughout each movement with three twin-axis goniometers and one single-axis torsionmeter (Figure 3.3) (models SG110/150 and Q110/Q150, respectively, Biometrics Ltd, Newport, UK) that were connected to an 8-channel MyoSystem data collection system (model 1400L, Noraxon, Scottsdale, AZ, USA). Data were sampled using the default system parameters which include 1 kHz frequency and 12 bit resolution. Individual movements were identified, segmented, averaged, and plotted using MATLAB software (The MathWorks, Natick, MA).



**Figure 3.3:** Biometrics twin-axis goniometer and single-axis torsiometer.

The angular displacements of interest are wrist flexion/extension, wrist abduction/adduction, elbow flexion/extension, shoulder horizontal flexion/extension, shoulder abduction/adduction, forearm supination/pronation and shoulder internal/external rotation. Sensors were applied using guidelines provided by the manufacturer's user manual and previous studies in upper extremity kinematics (Chao et al. 1980; Anglin and Wyss 2000; Hansson et al. 2004; Wise et al. 2004; Magermans et al. 2005; Biometrics 2010). Subjects were seated comfortably upright and the instrumented upper extremity was allowed to move freely within the task space while performing the motor tasks. This methodology was selected as it has been demonstrated as a successful method for studying upper limb joint motion and coordination during simulated ADLs (Chao et al. 1980; O'Neill et al. 1992).

The time to completion for the motor task and the variability with which it is performed are of particular interest throughout the dissertation. Prior work in the kinematics of human movement has established that the acquisition of a novel motor skill is accompanied with notable and progressive changes in several joint-level parameters (Darling et al. 1988; Gutman et al. 1993). It has been shown that early in the skill acquisition process, movement variability begins high due to irregular angular

displacement and velocity profiles, but continues to decrease and then plateau with continued practice (Flament et al. 1999; Smeets 2000). Movements with lower variability have been associated with better technique (Payton et al. 2007; Winter 2009). However, as will be discussed in Chapter 5, the acquisition of skills may be accompanied by the stabilization and destabilization of kinematic degrees of freedom. Further, decreased movement duration over consecutive movement trials has previously been shown to be an accurate measure for quantifying motor adaptation (Flament et al. 1999; Kempf et al. 2001; Smith et al. 2006). Motor skill performance can also be described by the intersegmental coordination between multiple body segments involved in the activity (Newell 1991; Kelso 1995; Newell et al. 2001). Continuous relative phase (CRP) has been used to investigate the intersegmental coordination of multiple body segments during rhythmic biological motions such as finger oscillation (Kelso 1984; Haken et al. 1985), wrist swinging (Rosenbaum and Collyer 1998), and juggling (Post et al. 2000). The CRP mean and standard deviation for a movement cycle are interpreted to be measures of coordination mode and coordinative stability, respectively (Lamoth et al. 2002).

### **Electromyography (EMG)**

For Specific Aims 1 and 3, surface EMG data of the biceps brachii, triceps brachii, anterior deltoid, and posterior deltoid were recorded (1 kHz sampling rate, filtered at 20-200 Hz) to inform of the onset of volitional movement. This method for determining the commencement of movement by monitoring EMG activity has been successfully implemented for the study of upper extremity reaching/grasping behavior (Perfiliev et al. 2010; Cos et al. 2011; Van Ooteghem et al. 2013), clinically relevant

exercises/assessments (Avila et al. 2013; Vaseghi et al. 2013), and motor development (van Balen et al. 2012). This particular EMG band-width has been used previously in the identification of movement onset in goal-directed upper extremity reaching movements (Mizelle et al. 2011). Additionally, EMG has been used in conjunction with EEG to study motor control of reaching, grasping, and tool use tasks (Wheaton et al. 2008b; Suzuki et al. 2010; Johnson et al. 2011; Demandt et al. 2012).

### **Trinity Amputation and Prosthesis Experience Scales (TAPES)**

For Specific Aims 1 and 2, average psychosocial adjustment of amputees to their prostheses was assessed by the TAPES survey (Appendix A); which contains questions including those related to disability-related variables, demographics, emotional well-being, pain, and coping (Gallagher and MacLachlan 1999). This set of evaluations has been successfully used to investigate quality of life and functionality in persons with limb deficiency in the contexts of therapeutic treatment for phantom limb pain (MacLachlan et al. 2004; McAvinue and Robertson 2011), coping strategies (Desmond and MacLachlan 2006), body image (Gallagher et al. 2007), and physical activity (Deans et al. 2008). There are multiple dimensions evaluated in the full TAPES survey: general adjustment, social adjustment, adjustment to limitation, functional restriction, social restriction, athletic activity restriction, weight satisfaction, functional satisfaction, and esthetic satisfaction. However, many of these assessments were designed in the context of persons with lower extremity amputation. The TAPES has been adapted for use in persons with upper extremity amputation (Desmond and MacLachlan 2005). Modifications to the TAPES include the removal of evaluative statements pertaining to experiences exclusive to persons with lower limb amputation such as “I don’t mind that people notice me



limping.” For this dissertation, particular focus was given to assessment of psychosocial adjustment. This metric evaluates how well a subject has adjusted to their prosthesis and incorporated it into their lives. Questions pertain to general life outlook, experiences in social situations, and the reaction to new limitations in activity and capability.

### **Minnesota Manual Dexterity Test (MMDT)**

For Specific Aim 3, subjects completed a modified version of the MMDT (Lafayette Instrument, Lafayette, IN, Appendix B) throughout the course of training in order to evaluate and track their FAMS-eye coordination and arm-FAMS dexterity. This test required subjects to actively open and close the terminal device via the cabling system and shoulder harness. The test involved using the FAMS terminal device to grasp and move six numbered disks from the numbered spots on the left side of a workspace board to matching numbered spots on the right side of the board and then back again. Subjects were instructed to perform the task as quickly and as accurately as possible. Each test comprised of three rounds of the task and the duration of each was recorded with a stopwatch. The MMDT has been used previously to study improvements in motor impairment during rehabilitation and motor task training in hemiplegic stroke survivors (Lourencao et al. 2005; Bhatt et al. 2007; Lourencao et al. 2008; Pandian and Arya 2013) and adults with cerebral palsy (Hutzler et al. 2013).

### **Pantomime Recognition Scale (PRS)**

For Specific Aim 1, in order to characterize subject movement quality while imitating the tool demonstrations, all movements were rated by a single evaluator according to the PRS (Appendix C). This scale was originally developed to evaluate the degree to which patients suffering from apraxia could effectively perform pantomime

movements (Wang and Goodglass 1992; Parakh et al. 2004; Crutch et al. 2007; Bickerton et al. 2012). It was later adapted for the use of evaluating pantomime performance in cognitive motor control studies, and is used in a similar context here (Wheaton et al. 2008a; Bohlhalter et al. 2009).

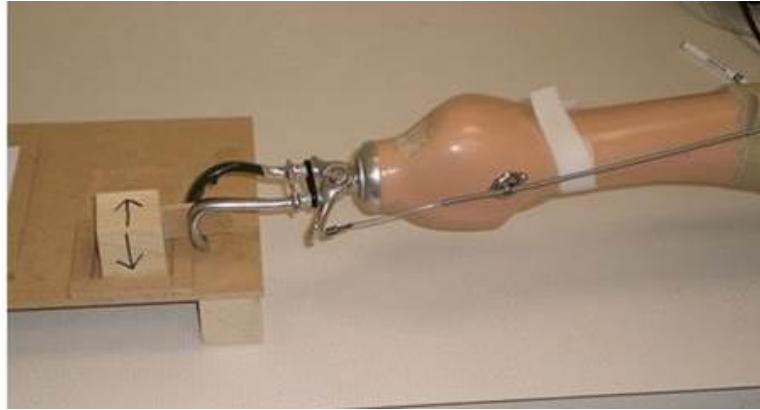
### **Experimental Motor Tasks**

The experimental motor tasks chosen for this dissertation represent a wide variety of operations that are emblematic of ADLs for intact individuals and persons with upper extremity limb amputations. Each task was selected in order to best address the questions posed by the respective specific aims. For Specific Aim 1, six tasks were chosen for the observation-imitation paradigm: switching a light switch, drinking from a water bottle, checking boxes with a pen, flipping a pancake with a spatula, shaking spices out of a dispenser, and turning a key in a lock. The use of unlike tools together was designed intentionally to elicit general tool related activation in the parietofrontal cortical regions (Moll et al. 2000; Hermsdorfer et al. 2007; Bohlhalter et al. 2009; Wheaton et al. 2009). This network has been shown to be responsible for action encoding of general tool-use, rather than for processing specific tool information (Jeannerod et al. 1995; Johnson-Frey 2004a; Mizelle and Wheaton 2010). The generalization of the specific tools observed in the videos allowed the investigation to focus on the effect of the arm type being imitated during movement planning.

For Specific Aim 2 and 3, a motor task was adapted from the clinically validated Southampton Hand Assessment Procedure (SHAP) which consists of both abstract object tasks and ADLs (Light et al. 2002). The block rotation task involves the rotation of a wooden cube 90° clockwise and then 90° counterclockwise while keeping the block

confined within a small target workspace (Figure 3.4). While this task is somewhat abstract, it serves as a surrogate for functionally relevant tasks such as turning a key in a lock or turning a door knob. Tasks such as these have been previously used to evaluate the function of upper extremity amputee prosthesis users (Metcalf et al. 2007; Ramirez et al. 2009).

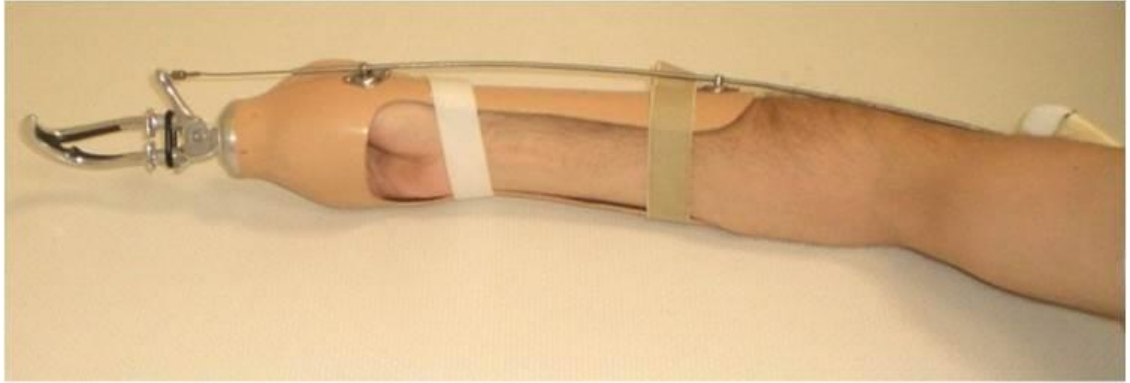
The block rotation task is comprised of two principal components: a rotation that permits the flipping of the block and a translation to control the end effector such that the block does not leave the workspace board target area. For intact individuals, this task configuration typically involves significant forearm pronation/supination, wrist flexion/extension, and wrist abduction/adduction. Each of these degrees of freedom are eliminated or severely limited by upper extremity amputation and thus, the task can be particularly difficult for prosthesis users. In order for prosthesis users to perform the observed task, they adapt alternative control strategies in the remaining degrees of freedom; likely involving modified joint behavior in the elbow and shoulder. While there are no clear methods for determining the success rate for this task, its cyclical nature is well suited for analysis of the accompanying ELGON data.



**Figure 3.4:** Block rotation motor task.

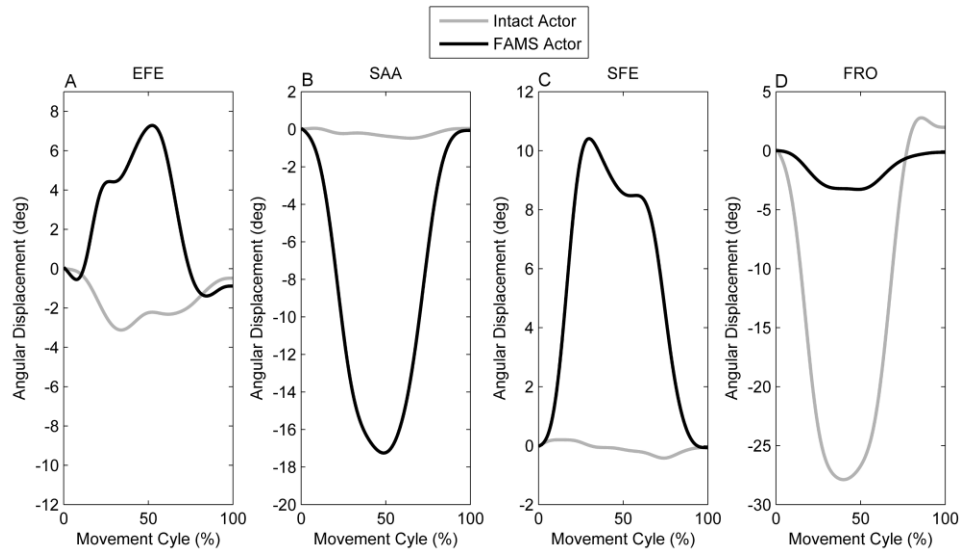
### **Fictive Amputee Model System (FAMS)**

This dissertation includes able-bodied subjects using a FAMS (Figure 3.5). The FAMS is a specially designed prosthetic device that fits over the limb of an intact subject. A hook-style terminal device is attached to the socket and is actuated via a body-powered harness. The mode of operation is similar to that which a person with transradial amputation would experience with their prosthetic device. In persons with amputations, the altered kinematics of the limb-prosthesis system necessitates the development of novel motor control strategies that yield unique movement characteristics (Bouwsema et al. 2010b; Losier et al. 2011). The FAMS allows an intact subject to simulate the eliminated or modified joint level degrees of freedom experienced by an upper extremity prosthesis user.



**Figure 3.5:** Fictive amputee model system (FAMS).

The intended effect of this device is demonstrated in Figure 3.6, which shows the movement kinematics of an intact subject first using their natural limb to complete the block rotation task, and then repeating the task while using the FAMS. These data show the near elimination of forearm pronation/supination during task performance with the FAMS (Figure 3.6D). Correspondingly, shoulder abd/adduction (Figure 3.6B) and flexion/extension (Figure 3.6C) demonstrate increased range of motion in order to facilitate the completion of the task. Finally, movements performed with the FAMS are slower compared to movements with the intact limb. With fewer degrees of freedom at their disposal, we are suggesting that both amputees and intact FAMS users adopt alternate joint coordination strategies in order to successfully complete motor tasks.



**Figure 3.6:** Effect of FAMS on performance of block rotation task in elbow flexion/extension (EFE), shoulder abd/adduction (SAA), shoulder flexion/extension (SFE), and forearm supination/pronation (FRO).

Access to appropriate amputee subjects is limited and should be recruited judiciously when populating a study. Additionally, controlling for factors such as original handedness, amputation side, amputation level, time since amputation, and experience with a prosthesis further reduces the pool of appropriate subjects. Therefore, in order to best utilize these subjects, the details of prosthesis training protocols should be fully developed before evaluating in amputees. Laying the foundation for this effort using the FAMS in intact subjects is advantageous as it will facilitate the rapid testing and refinement of training protocols prior to the recruitment of amputees. Recruiting intact subjects is substantially more practical than recruiting amputees, and thus will accelerate progress. This strategy permits the evaluation of the potential benefits of matched-limb clinical training in a controlled paradigm. Devices such as the FAMS have been previously used in intact subjects to investigate modes of prosthesis control (Bouwsema

et al. 2010a) and the design of prosthesis training protocols (Bouwsema et al. 2008; Smurr et al. 2008).

The comparison of FAMS results with those of persons with limb deficiency must be carefully considered due to the fact that the latter have amputations, whereas the former are intact subjects. The degree to which the motor cortex is affected by amputation is substantial on a number of important levels. However, the focus of this dissertation is on the motor-related action encoding areas in the frontal, parietal, and occipital cortices that are engaged when planning and executing tool-use pantomime movements.

Strictly speaking, a prosthesis is defined as an artificial replacement of a body part (Bowker et al. 2002), while an orthosis is defined as a device applied to a human limb to control or enhance movement (Hsu et al. 2008). Thus, while the FAMS has the appearance and functionality of a prosthesis, it interfaces with the subject more accurately as an orthosis. Specifically, the FAMS eliminates all movement of the wrist and restricts movement of the forearm. Further, since the FAMS is placed over an intact limb, the length and mass of the limb and FAMS together is greater than that of a person with amputation wearing a comparable prosthesis. These differences in mass and length will have an effect on the kinetic and kinematic properties of the movements. For this reason, no comparisons of the movement kinematics are made between FAMS users and persons with amputation using a prosthesis.

Beyond the movement restrictions of the FAMS device itself, the overall movement is additionally constrained by the workspace surrounding the subject. Specifically, subjects were not permitted to touch the chair or table with their arm while

performing the task. Finally, the FAMS is secured on a subject's arm by compression provided by Velcro straps. It should be noted that variability in limb soft tissue volume and composition across subjects changes the fit of the FAMS. Therefore, additional padding was provided within the socket to accomplish the tightest individualized fit possible for each subject.



# **CHAPTER 4**

## **NEURAL ACTIVATION DIFFERENCES IN AMPUTEES DURING IMITATION OF INTACT VERSUS AMPUTEE MOVEMENTS**

### **Introduction**

Previous studies document that specific areas within the premotor, motor, and parietal cortices are activated when planning, executing and observing cognitive motor control tasks (Cattaneo and Rizzolatti 2009). This parietofrontal network may provide a mechanism by which we can understand, learn, and imitate the actions of others from our own perspective (Rizzolatti and Sinigaglia 2010). Recent work shows that the mirror neuron system observation effects may be weakened when an individual witnesses a human movement performed by a virtual robotic actor with human-like kinematics. This result suggests that the mirror neuron system may be preferentially engaged by limb movements that are similar in appearance and kinematic capabilities to that of the viewer. Evidence also shows sensitivity of the mirror neuron system based on whether the observed action is possible for the observer to perform. It has been shown that observing non-conspecific actions that are not possible in humans activates bilateral visual responses instead of action encoding areas (Wheatley et al. 2007). These results may suggest a different encoding mechanism for the observation of actions performed with dissimilar limb types.

The goal of this chapter is to investigate whether neural activations during planning and execution in persons with amputation vary as a function of the type of limb

they see performing an action. This was investigated with EEG by instructing both intact subjects and prosthesis users to imitate tool use movements observed in video demonstrations featuring an intact actor or prosthesis user. We hypothesized that the neural activations of intact subjects would not be affected by the video demonstration type, but that those of the prosthesis users would be. Specifically, prosthesis users imitating another prosthesis user would preferentially activate the parietofrontal network, consistent with tool use neural activity with an existing motor template that should exhibit stronger resonance with the action. Contrastingly, prosthesis users imitating an intact individual would activate the parietooccipital network, in addition to the typical parietofrontal regions. This would reflect the increased visuospatial demands of imitating the movements of a dissimilar limb without a readily available motor template. If additional occipitoparietal activation is required in mismatched limb imitation, this would reveal unique action planning strategies in prosthesis users. These atypical strategies may relate to the challenges experienced by amputees while developing action representations that incorporate a prosthesis.

## **Methods**

### **Subjects**

Ten right-handed intact subjects were recruited for this study (4 female, 6 male, mean age:  $24.8 \pm 3.3$  years, range: 23-34 years). Six upper extremity amputee prosthesis users were also recruited (2 female, 4 male, mean age:  $44.3 \pm 9.9$  years, range: 33-59 years). Signed informed consent was acquired from all subjects according to the procedures set forth by the Institutional Review Board at The Georgia Institute of Technology. The Edinburgh Handedness Inventory (Appendix D) (Oldfield 1971) was

use to confirm the handedness of the intact subjects and, in the case of amputees, recalled handedness prior to their amputation. Amputee subjects reported wearing their prosthetic devices an average of  $4.4 \pm 3.6$  hours/day. Average psychosocial adjustment of the amputees to their prostheses, as assessed by the TAPES survey (Desmond and MacLachlan 2005), was calculated to be  $51.6 \pm 9.0$  (on a scale from 14-70, with higher values indicating greater adjustment). Before being recruited into the protocol, all subjects were screened for the presence of any other neurologic factors, including (but not limited to) traumatic brain injury, stroke, or concussion. The presence of phantom limb syndrome/pain was an exclusion criterion for the amputee subjects. The amputee population was made up of persons who had lost their limb due to occupational and recreational accidents with no brain trauma. Demographic and clinically relevant information for the prosthesis users is presented in Table 4.1. Notably, with the exception of one especially chronic amputee, the amputee subjects had experienced their amputations within a similar time frame (0.6 – 3.5 years) and they had also been using their current prosthetic devices for a similar time frame (0.3 – 2.3 years) (Table 4.1).

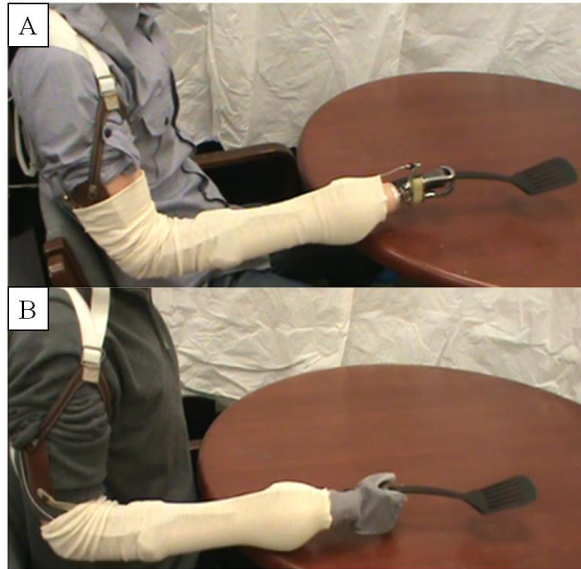
**Table 4.1:** Demographic and clinically relevant information for the prosthesis users. A=ambidextrous, Dom=dominance, Amp=amputation, TRAU=traumatic, TR=trans, ED=elbow disarticulation, PX=prosthetic device type, Body=body powered, Myo=myoelectric, TD=terminal device, NR=not reported, PAS=Psychosocial Adjustment Scale (on a scale from 14-70, with higher values indicating greater adjustment).

	Sex	Age (yrs)	Hand dom	Amp cause	Level	Amp side	Yrs since amp	Yrs since 1 <sup>st</sup> PX	Yrs with current PX	Power type	TD	PX use (hrs/day)	PAS
Pro1	F	53	R	TRAU	TR	L	17.0	16.8	16.8	Body	Hook	0	52
Pro2	M	59	A	TRAU	TR	R	4.5	3.5	1.0	Myo	Hand	4	56
Pro3	M	33	R	TRAU	TR	R	0.8	0.6	0.3	Myo	Hook	10	39
Pro4	M	44	R	TRAU	TR	R	2.5	2.3	2.3	Body	Hook	NR	NR
Pro5	M	38	R	TRAU	ED	R	2.5	2.3	1.3	Body	Hook	3	63
Pro6	F	39	R	TRAU	TR	R	3.3	2.0	1.0	Myo	Hand	5	48
Mean $\pm$ SD	---	44.3 $\pm$ 9.9	---	---	---	---	5.1 $\pm$ 6.0	4.6 $\pm$ 6.1	3.8 $\pm$ 6.4	---	---	4.4 $\pm$ 3.6	51.6 $\pm$ 9.0

## **Procedure**

Subjects were fitted with a 58-channel EEG cap (Electrocap, Eaton, OH) that recorded scalp potential activity (1 kHz sampling rate, filtered at DC-100 Hz) via the Synamps 2 data acquisition system (Compumedics Neuroscan, Charlotte, NC). For analysis, EEG data was further pass-band filtered from DC-30 Hz. Electrooculography was recorded in two locations near the left eye to monitor eye blinks and movements. Surface EMG data (1 kHz sampling rate, filtered at 20-100 Hz) of the biceps brachii, triceps brachii, anterior deltoid, and posterior deltoid were recorded to inform of the onset of volitional movement.

Subjects were seated 1.5 m away from a computer screen that displayed videos of tool use movements followed by written directions regarding the movement tasks to be performed. All subjects viewed video demonstrations of common tools being used by both an intact actor and an actor wearing a body powered prosthetic device. In the case of prosthesis users, the terminal device featured in the video matched that of the subject. A Model 5X Hook (Hosmer, Campbell, CA) was used for those subjects with a voluntary opening, split hook type terminal device (Figure 4.1A) while a simple articulated anthropomorphic hand was used for those subjects with a hand-type terminal device (Figure 4.1B). Intact subjects only viewed the Model 5X Hook terminal device.



**Figure 4.1:** Prosthetic limb terminal devices used in tool use video demonstrations: Hosmer Model 5X Hook (A) and simple articulated anthropomorphic hand (B).

After the presentation of each video, all subjects were instructed to imitate the action they had seen in the video by pantomime. Intact subjects performed the task with their dominant arm and amputees used their prosthetic device. The prosthesis users were not required to perform active prehension with their terminal devices in order to successfully pantomime the observed movements. There were four experimental groups: intact subjects imitating an intact actor (Int-Int), intact subjects imitating a prosthesis user (Int-Pro), prosthesis users imitating an intact actor (Pro-Int), and prosthesis users imitating a prosthesis user (Pro-Pro). There were six tool use tasks performed in the video demonstrations. In three tasks, an intact actor performed switching a light switch, drinking from a water bottle, and checking boxes with a pen. In the remaining three tasks a prosthesis user performed flipping a pancake with a spatula, shaking spices out of a dispenser, and turning a key in a lock. The videos were presented in an alternating order

such that each successive video displayed a demonstrator arm type different than the previous. Each video was shown for 60 s and contained exactly 6 movement repetitions.

After watching each video, subjects performed tool use motor tasks that were visually cued using Stim (Compumedics Neuroscan, Charlotte, NC). Subjects fixated on a white cross for a randomly determined baseline period of 4.0-6.0 s. Subjects were then instructed to remain motionless and begin planning for the movement upon seeing a “Get Ready!” cue for 1.0 s. Immediately afterward a final cue appeared commanding them to “Move!” which remained on the screen for 4.0 s. During this period, subjects were instructed to imitate the movement they observed in the video by pantomiming the action. For technical reasons, it was not possible for each movement cue to be preceded by a repetition of the video demonstration. This cued movement sequence was repeated 50 times for each of the six demonstrations, for a total of 300 movements per data collection. All subjects were periodically allowed rest sessions between movement trials to mitigate effects related to fatigue. Presentation of the “Move!” cue is aligned with the zero point on the timeline. The 1.0 s preceding this cue is referred to henceforth as the movement planning phase while the period of time after this cue is referred to as the movement execution phase. To characterize the movement quality of the two subject populations imitating the tool demonstrations, all movements were rated by a single evaluator according to the PRS (Appendix C, maximum score 4) (Wheaton et al. 2008a; Bohlhalter et al. 2009).

### **Data Recording and Analysis**

Using Scan4.5 (Compumedics Neuroscan, Charlotte, NC), continuous EEG data were epoched to 3.1 s epochs centered on the presentation of the “Move!” cue (-1.6 s to

1.5 s) and linear detrended. Baseline correction between -1.6 s to -1.1 s relative to the “Move!” cue was then performed. A combination of artifact averaging and regression analysis was employed to remove ocular artifacts (Semlitsch et al. 1986). A final visual inspection was performed and any epoch containing data that was outside a threshold range of -100 to 100  $\mu$ V was rejected. Individual subject data was then averaged across individual tool type and grouped into the four experimental conditions described previously. The grouping of unlike tools together was designed intentionally to elicit general tool related activation in the parietofrontal cortical regions (Moll et al. 2000; Hermsdorfer et al. 2007; Bohlhalter et al. 2009; Wheaton et al. 2009). This network has been shown to be responsible for action encoding of general tool-use, rather than for processing specific tool information (Jeannerod et al. 1995; Johnson-Frey 2004a; Mizelle and Wheaton 2010). The generalization of the specific tools observed in the videos allowed the investigation to focus on the effect of the arm type being imitated during movement planning.

Statistical analysis and plotting were then performed using MATLAB software (The MathWorks, Natick, MA). All epochs were averaged into 100 ms timebins and further grouped into the regions of interest that were defined in the left and right premotor areas (LPM: F3, F1, C5A, C3A, C1A; RPM: F4, F2, C6A, C4A, C2A), left and right motor areas (LM: C5, C3, C1; RM: C6, C4, C2), left and right parietal areas (LP: TCP1, P5, P3, P1, P3P; RP: TCP2, P6, P4, P2, P4P), and occipital area (OCC: O1, OZ, O2) (Wheaton et al. 2005b). To enhance our ability to capture the timing of differences in the neural signal, t-tests were performed across 100 ms voltage timebins from the onset of the planning cue through 1.5 s after the move cue. Four statistical comparisons were

performed in this analysis. The first pair of statistical analyses evaluated the effect of the video demonstration type within each subject type (Int-Int vs. Int-Pro; Pro-Pro vs. Pro-Int). The next pair of statistical analyses evaluated the effect of subject arm type within each video demonstration type (Int-Int vs. Pro-Int; Int-Pro vs. Pro-Pro). This latter set of comparisons is particularly salient due to the consistency of the tool movements being imitated within each subject type. The threshold for statistical significance was held at  $\alpha=0.001$  for all comparisons. This level of significance has been used previously in EEG studies of upper extremity movement imagery, planning, and execution (Yuan et al. 2010a; Yuan et al. 2010b; Deiber et al. 2012). To avoid misinterpretation of spurious cortical activity differences and to ensure that the differences observed are not transient, statistically significant differences between groups must be maintained for four consecutive timebins (400 ms).

Filtered EMG data were averaged together within each subject and experimental condition. For each set of movements, baseline EMG activity was defined as the mean activity of the 500 ms preceding the movement cue. EMG onset occurred once the activity surpassed two standard deviations of the baseline mean for a period of at least 25 ms. Statistical t-tests were performed within each muscle type to determine if the intact subjects and prosthesis users initiated EMG onset at different time intervals when performing imitations of the same tool types. The threshold for statistical significance was held at  $\alpha=0.001$ . Table 2 shows the average EMG onset times and p-values for each of the four muscles recorded for the following comparisons: Int-Int vs. Pro-Int and Int-Pro vs. Pro-Pro. Further, in order to investigate whether the EMG onsets were affected by either of the experimental variables, multivariate ANOVAs were performed with subject



group (2) and muscle type (4) as factors. In order to control for the tool use movements being imitated, separate ANOVAs were performed on the pairs of groups that imitated intact actors (Int-Int; Pro-Int) and prosthesis users (Int-Pro; Pro-Pro). The threshold for statistical significance was held at  $\alpha=0.05$  for all ANOVAs.

## **Results**

### **EMG and Movement Quality**

The results show that there were no differences between the overall EMG onset times between the intact subjects and prosthesis users within each muscle (Table 2). Further, an ANOVA comparing muscle activation onset for Int-Pro vs. Pro-Pro did not show a main effect for specific muscle ( $F=2.67$ ,  $p=0.06$ ), subject arm type ( $F=0.22$ ,  $p=0.64$ ), or an interaction between the two factors ( $F=0.31$ ,  $p=0.82$ ). However, an ANOVA analysis comparing Int-Int vs. Pro-Int revealed a main effect on EMG onset for specific muscle ( $F=2.38$ ,  $p=0.04$ ), but not for subject arm type ( $F=3.62$ ,  $p=0.06$ ), or an interaction between the two factors ( $F=1.15$ ,  $p=0.34$ ). While not statistically significant, a difference in EMG onset order was observed. The Int-Int, Int-Pro and Pro-Pro groups show a common sequence of EMG onset in the following order: anterior deltoid, biceps brachii, triceps brachii, posterior deltoid. The Pro-Int group shows the following unique pattern of EMG onset: biceps brachii, anterior deltoid, posterior deltoid, and triceps brachii.

For the intact video imitations, intact subjects received significantly higher PRS scores (Int-Int,  $4.0 \pm 0.0$ ) than the prosthesis users (Pro-Int,  $3.35 \pm .58$ ) ( $p < 0.001$ ). Similarly, for the prosthesis video imitations, intact subjects received significantly higher PRS scores (Int-Pro,  $4.0 \pm 0.0$ ) than the prosthesis users (Pro-Pro,  $2.83 \pm .47$ ) ( $p < 0.001$ ).

**Table 4.2:** Electromyography (EMG) onset data. Average EMG onset times for intact subjects and prosthesis wearers imitating same tool type. Statistical t-tests were performed within muscle type to investigate if EMG onset was different between the two subject populations. Significance threshold was held at  $\alpha=0.001$ .

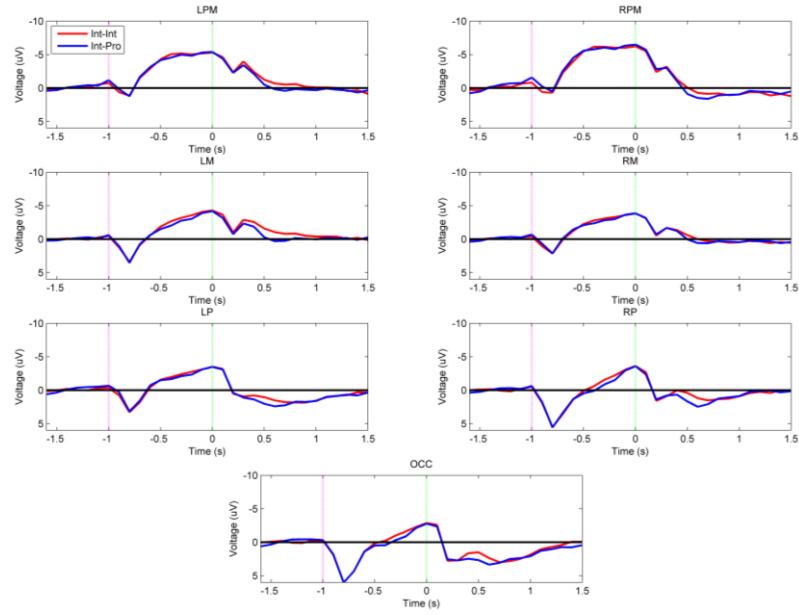
	Average EMG onset $\pm$ SD (s)			Average EMG onset $\pm$ SD (s)		
	Int-Int	Pro-Int	P-value	Int-Pro	Pro-Pro	P-value
<b>Biceps brachii</b>	238.5 $\pm$ 75.8	207.5 $\pm$ 118.5	0.540	251.0 $\pm$ 106.7	265.8 $\pm$ 116.4	0.809
<b>Triceps brachii</b>	329.1 $\pm$ 106.4	281.3 $\pm$ 135.8	0.487	329.9 $\pm$ 132.1	275.4 $\pm$ 93.2	0.428
<b>Ant. deltoid</b>	205.6 $\pm$ 63.2	210.2 $\pm$ 64.4	0.901	198.3 $\pm$ 56.5	218.0 $\pm$ 86.1	0.644
<b>Pos. deltoid</b>	353.4 $\pm$ 123.3	215.6 $\pm$ 98.6	0.058	372.9 $\pm$ 170.1	326.8 $\pm$ 136.9	0.640

## Neural Outcomes

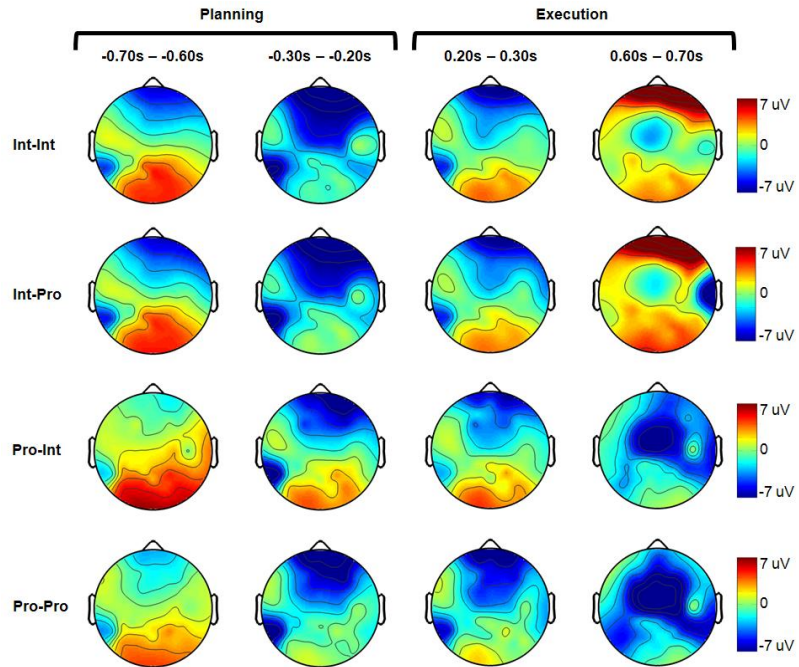
### Effect of Video Demonstration Arm Type

Figure 4.2 shows the grand-averaged voltage plots for the comparison between intact subjects imitating both intact actor and prosthesis user demonstrations (Int-Int vs. Int-Pro). There was no effect of demonstration arm type on the imitation neural activations of intact subjects during movement planning or execution ( $\alpha=0.001$ ). Both groups exhibited the same pattern of high left parietal and mesial frontal negativity during movement planning and motor region negativity during movement execution as shown in Figure 4.3.

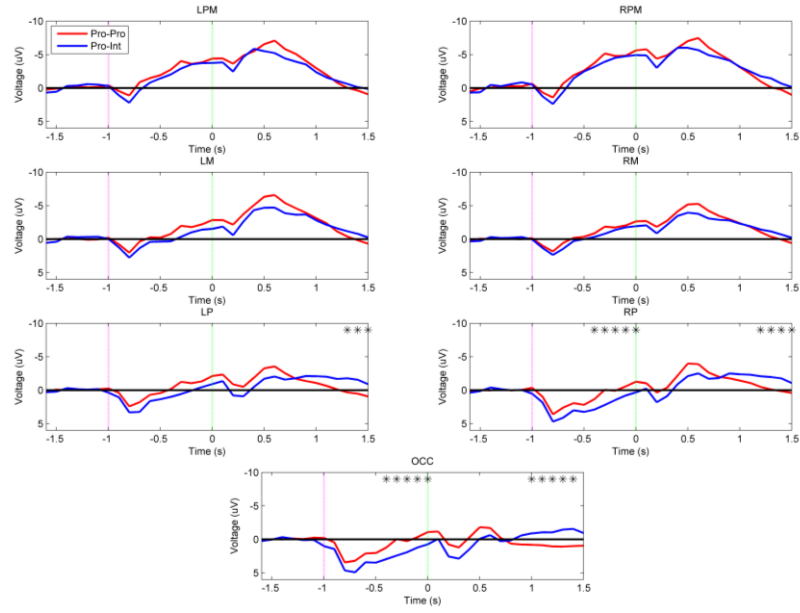
In contrast to the intact group, Figure 4.4 shows that there is an effect of demonstration arm type on the neural activations of prosthesis users (Pro-Pro vs. Pro-Int). The Pro-Int group (arm type mismatched) showed significantly greater positivity ( $p<0.001$ ) during movement planning in the right parietal (-400 ms to 0 ms) and occipital regions (-400 ms to 0 ms).



**Figure 4.2:** Grand-averaged region-level voltage plots for the Int-Int (red) and Int-Pro (blue) groups. The planning cue is marked with a pink dotted line at -1.0 s and the execution cue is marked with a green dotted line at 0.0 s. Time bin voltage values that are statistically different between the two groups are marked with asterisks.



**Figure 4.3:** Grand-averaged electrode headplots for all experimental conditions. For each condition, four representative 100 ms timebins are shown. The planning and execution phases are marked above.

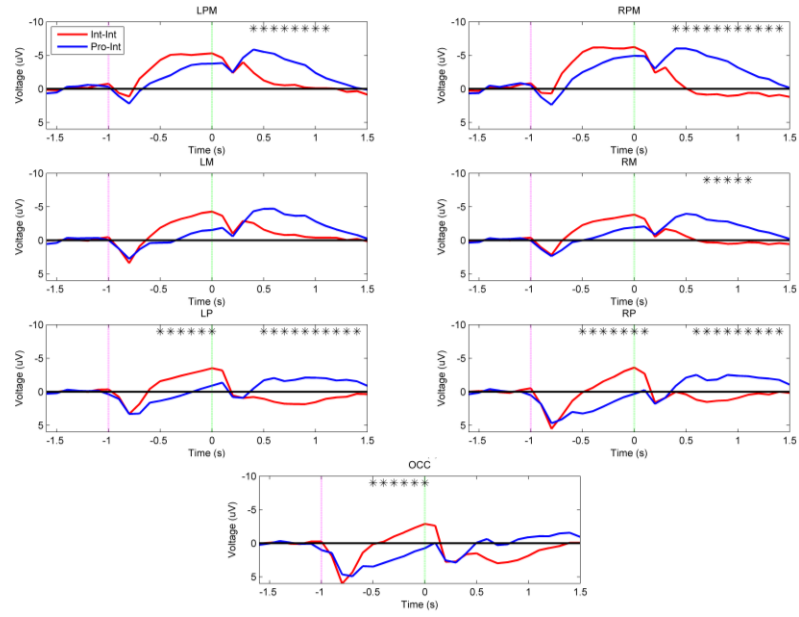


**Figure 4.4:** Grand-averaged region-level voltage plots for the Pro-Pro (red) and Pro-Int (blue) groups. The planning cue is marked with a pink dotted line at -1.0 s and the execution cue is marked with a dotted line at 0.0 s. Time bin voltage values that are statistically different between the two groups are marked with asterisks.

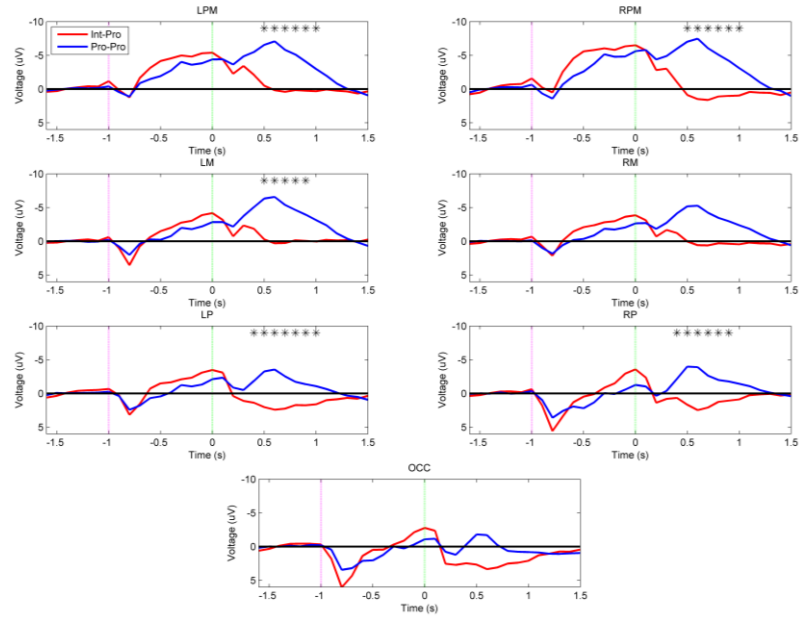
### Effect of Subject Arm Type

To establish that differences in subject arm type are the principal contributors to the observed planning related cortical activation patterns, the next two comparisons were performed between intact subjects and prosthesis users who were both prompted by the same set of tool use movements. Figure 4.5 demonstrates that there was an effect of subject arm type when both groups imitated the intact video demonstrations (Int-Int vs. Pro-Int). The Pro-Int group showed significantly greater positivity ( $p < 0.001$ ) during movement planning and early execution in the bilateral parietal (-500 ms to 100 ms) and occipital regions (-500 ms to 0 ms).

Figure 4.6 reveals that the arm type mismatch planning differences are mitigated when a prosthesis user imitates another prosthesis user (Int-Pro vs. Pro-Pro). In this comparison, amputees who imitated a matched arm type showed no significant neural differences from intact subjects during the movement planning phase ( $\alpha = 0.001$ ). This pattern was also apparent when comparing the Int-Pro vs. Pro-Pro group headplots in Figure 4.3. Differences between these two groups were seen during execution. Compared to the intact subjects, the prosthesis users showed greater negativity ( $p < 0.001$ ) in the bilateral premotor (500 ms to 1000 ms), left motor (500 ms to 900 ms), left parietal (400 ms to 1000 ms), and right parietal regions (400 ms to 900 ms) during execution (Figure 4.6).



**Figure 4.5:** Grand-averaged region-level voltage plots for the Int-Int (red) and Pro-Int (blue) groups. The planning cue is marked with a pink dotted line at -1.0 s and the execution cue is marked with a dotted line at 0.0 s. Time bin voltage values that are statistically different between the two groups are marked with asterisks.



**Figure 4.6:** Grand-averaged region-level voltage plots for the Int-Pro (red) and Pro-Pro (blue) groups. The planning cue is marked with a pink dotted line at -1.0 s and the execution cue is marked with a green dotted line at 0.0 s. Time bin voltage values that are statistically different between the two groups are marked with asterisks.



## Discussion

For this chapter, intact subjects and upper extremity amputee prosthesis users were recruited to view and imitate video demonstrations of tools being used by an intact actor and a prosthetic device user. The intact subjects showed equivalent left parietal and mesial frontal activation for imitating both the intact or prosthetic limb. However, when prosthesis users imitated intact subjects, greater right parietal and occipital activation during planning was observed in addition to parietofrontal activation. Prosthesis users who imitated other prosthesis users showed only the typical left parietal and mesial frontal activation. This finding suggests that prosthesis users can engage the anticipated left hemispheric planning related activity and disengage the parietooccipital system when they imitate a limb state that matches their own. The limb imitation effects seen in the amputees suggest the additional involvement of unique planning mechanisms while using their prosthetic device. This result has implications on how device operation is conveyed to amputees during rehabilitation.

The interpretation of execution phase cortical activity comparisons across groups is limited by a number of factors. Most significantly, amputees require a different number, combination, and activation level of muscles in order to complete the movement task with their residual limb (Schabowsky et al. 2008; Velliste et al. 2008; Metzger et al. 2010). The altered kinematics and kinetics of the limb-prosthesis system also necessitate the development of novel motor control strategies that yield unique movement characteristics in amputees (Bouwsema et al. 2010b; Losier et al. 2011). Such physiological and functional variations may account for the significantly lower PRS scores received by prosthesis users compared to intact subjects. However, a limitation of

the current study is the lack of a direct link between the observed cortical activation changes and the explicit motor performance of the tasks. The effect of atypical cortical action encoding strategies on motor task performance is presently being investigated.

With the exception of one especially chronic amputee, the amputee subjects had experienced their amputations within a similar time frame. Typically, significant time (several months) will elapse between the amputation and the first delivery of a prosthesis (Reinkensmeyer et al. 2012). This time delay is due to the slow progression of the healing process post-amputation. Once sufficiently recovered from the surgery, substantial time is also required in order to properly customize and fit the device to the user. Therefore, the subjects recruited for this work are considered to be in the early stages of their prosthesis use. Acquisition of amputees at a more acute level is impractical. Further, many of the amputee subjects had recently received new prosthetic devices that would require an additional adjustment period for functional use. Importantly, subjects were recruited that were no longer experiencing phantom limb syndrome or pain. These symptoms can persist for months or years following the initial wound healing (Conditt et al. 1997; Bouwsema et al. 2008). Thus, it was necessary to recruit from a relatively chronic amputee population in order to meet these exclusion criteria. The characterization of the time course of amputee adjustment to their prostheses is currently being investigated. Additionally, given the preliminary scope of this study, the low number of amputee subjects is justifiable as we were seeking to select a very selective, but relatively homogenous cohort of amputees. The number of subjects in the current study is comparable to the majority of research on the upper extremity amputee population (Montoya et al. 1998; Schaefer et al. 2002; Karl et al. 2004a; Karl et al. 2004b).

Further, sets of unlike tool demonstrations were grouped together into two categories: those demonstrated in the videos by an intact actor and those demonstrated by a prosthesis user. For example, in the comparison of Int-Int vs. Int-Pro, the intact subjects in each group are imitating different tool use movements. This logic is common for analysis for this task type, as the parietofrontal tool network seems to encode actions for general tool use rather than for specific tools (Jeannerod et al. 1995; Johnson-Frey 2004a). As such, the interpretation of execution phase cortical activity is difficult as a result of the muscle activations and joint coordination required for each of the unique tool-use tasks. Notably, in the example comparison cited above (Int-Int vs. Int-Pro), the cortical activations during execution were statistically equivalent despite the different tool movements being performed. It is reasonable to state that the differences observed in execution phase cortical activations for the Pro-Int vs. Pro-Pro comparison are most likely due to the differences in video demonstration arm type and not the type of tool movement imitated. Nonetheless, for the reasons stated above, the focus of this discussion is on the planning phase cortical activity prior to movement onset.

### **Action Planning in Intact Subjects**

Intact subjects showed no significant neural activation differences when imitating two dissimilar arm types. The equivalent left parietal and mesial frontal activity during planning in these subjects is characteristic of typical tool use pantomime activity (Goldenberg 2003; Fridman et al. 2006; Goldenberg et al. 2007; Hermsdorfer et al. 2007; Tsuda et al. 2009). The activity over the primary motor and parietal cortex during execution is attributable to the demands of performing the motor task and accessing tool use related knowledge, respectively (Johnson-Frey 2003; Glover 2004; Wheaton et al.

2005a; Wheaton et al. 2005c; Buxbaum et al. 2006; Creem-Regehr 2009). These results suggest that intact subjects are not sensitive to neurobehavioral variations when imitating the highly dissimilar prosthetic limb. Movement planning and execution proceed with no statistical differences, regardless of the state of the arm viewed in the demonstration. We propose that for intact subjects, the task goal is the most salient aspect of the viewed action; observation of which will result in parietofrontal activation related to action encoding (Caggiano et al. 2011; Vingerhoets et al. 2011). Therefore, the normal left parietal, mesial frontal and motor cortex mechanisms are engaged to an equivalent extent for both conditions, despite the differences in conspecifics of the demonstration arm types. This result supports recent evidence describing the normal action encoding system as end-effector independent (Rochat et al. 2010; van Elk et al. 2011).

## **Action Planning in Prosthesis Users**

### Prosthesis Users Imitating Intact Demonstrations

The Pro-Int group showed increased right parietal and occipital positivity in addition to the typical parietofrontal negativity during movement planning compared to the Pro-Pro group. We argue that due to the mismatch of the subject's arm with that of the video demonstration, the planning phase can no longer proceed as normal. In this case, the movement observed in the demonstration of an intact limb may not solely engage the classical mirror neuron system (Rizzolatti and Craighero 2004). It is proposed that this functional incongruity results in the increased visuospatial demand of the task and thus, requires additional parietooccipital activity to facilitate task performance (Buccino et al. 2004a).

There is precedence establishing that action encoding mechanisms may exist outside of the standard parietofrontal mirror neuron network. It has been proposed that the mentalizing system, which is important for understanding the intents of others, may be a candidate to serve this role when observing non-conspecific actions (Wheatley et al. 2007). Using this logic, the mentalizing system is engaged if no pre-existing motor template for the observed behavior exists (Van Overwalle and Baetens 2009). In this case, enhanced visual comprehension is required to convert the non-conspecific action into one that can be completed successfully. Under the mentalizing model, amputees may be able to recognize the task goal, but are unable to quickly develop new motor patterns for controlling their prosthetic device and rely on additional visual mechanisms for planning the movement. Thus, when prosthesis users imitate an intact subject, the muscle onset order may be affected; potentially reflecting a diminished resonance for the action (Strafella and Paus 2000; Funase et al. 2007; Alaerts et al. 2009). This mentalizing concept is corroborated by recent work demonstrating engagement of the mentalizing system in a congenital amputee when observing and imitating the actions of intact subjects (Aziz-Zadeh et al. 2012). Previous studies also suggest abnormal visuomotor processing demands for reaching tasks in amputees (Metzger et al. 2010). Presumably, this pattern of visuomotor conversion activity would continue until an appropriate motor template could be created (Mizelle et al. 2011). Investigation is ongoing to determine when and how the mirror neuron system may be engaged after such an update is completed.

### Prosthesis Users Imitating Other Prosthesis Users

Uniquely, when imitating prosthesis user demonstrations, there are no statistically significant differences between intact subjects and prosthesis users in right parietal or occipital areas during movement planning. This supports our proposal that the neural planning activations in a prosthesis user can resemble that of an intact subject, as long as there is an arm type match for the prosthesis user. According to the ideomotor principle, representations of actions are stored in the form of their effects. A bidirectional connection between an action and its effects is established through the association of one's own motor repertoires with the observed effects of the action (Hommel et al. 2001; Wohlschlaeger et al. 2003; Hommel 2009). The motor repertoires of amputees may have been updated to include their prosthesis via the accumulation of experience observing the effects of actions performed with the device.

We propose that, due to the matching limb state, the prosthesis users' action representations are more strongly engaged by observing the actions of other prosthesis users. The unique cortical activity patterns reported in this study during imitation of a mismatched limb may be a result of the observer's motor repertoires converging towards the prosthetic limb, while diverging away from that of the amputated biological limb. This proposed divergence may be observed in the EMG onset results, which also suggest that the Pro-Pro (limb match) group converges to the intact limb pattern while the Pro-Int (limb mismatch) group exhibits a unique pattern. Recent work has demonstrated that the motor system is capable of incorporating non-biological components (tools) to complete a task while commonly activating the mirror neuron system structures responsible for use of the hand by itself (Umiltà et al. 2008). As the prosthesis is integrated into the amputee

motor repertoire, the matching prosthetic limb video demonstration may preferentially engage the parietofrontal activity typically seen in intact subjects with normal motor repertoires, thus decreasing the dependence on additional processing support from the parietooccipital regions.

The similarities between intact subjects and prosthesis users when imitating prosthesis users (Int-Pro vs. Pro-Pro) appear to be confined to the planning phase. Once in the movement execution phase, the prosthesis users generally show higher negativity than the intact subjects in bilateral premotor, left motor, and bilateral parietal areas. This effect is a focus of ongoing task performance studies using EMG and ELGON.

### **EMG and Movement Quality**

The EMG onset data suggest that all experimental groups initiated EMG onset after a consistent period of time following the movement cue. While not statistically significant, a potential difference in muscle recruitment order was observed. Despite the differences in tool imitation movements, both intact subject groups (Int-Int, Int-Pro) reveal a consistent order of muscle activation. This pattern proceeds with a pattern of shoulder flexion (anterior deltoid), elbow flexion (biceps brachii), elbow extension (triceps brachii), and shoulder extension (posterior deltoid). For prosthesis users, this pattern is observed only when they imitate other prosthesis users. Otherwise, when a prosthesis user imitates an intact actor, a different pattern of EMG onset emerges: flexion of the elbow (biceps brachii), flexion of the shoulder (anterior deltoid), extension of the shoulder (posterior deltoid), and extension of the elbow (triceps brachii). These observations potentially suggest that the kinematics and kinetics of tool use movement in prosthesis users may be influenced by the type of limb being imitated. Understanding the

motor control and biomechanics of movement during task execution in prosthesis users is a focus of ongoing studies. Utilizing more sensitive techniques such as intramuscular EMG and kinematic assessments may improve our interpretation of these outcomes.

### **Conclusion**

The results of this chapter have implications on the design and implementation of rehabilitation and occupational therapy protocols for amputees. The current standard of amputee rehabilitation with intact occupational therapists may necessitate atypical planning mechanisms while learning to use their prosthetic device based on instruction by an intact therapist. The findings suggest that amputees may engage atypical planning mechanisms as they use their prosthetic device during any imitation-based therapy. This activity may be a reflection of the difficulty of the subject to easily translate the therapist's actions into their own actions. Results of the study suggest that while the neural activations of intact subjects seem to not differ when imitating movements performed by actors with different arm types, prosthesis users are susceptible to arm type. However, it is possible to elicit typical left parietofrontal cortical activation patterns in prosthesis users during imitation planning, provided they imitate other prosthesis users as opposed to intact actors. This effect may be accompanied by modification in the muscle activation patterns during execution of the movements. Therefore, the next chapter will address similar questions to investigate motor behavioral effects of mismatched limb imitation in new users of a prosthetic device.



# **CHAPTER 5**

## **MOTOR PERFORMANCE BENEFITS OF MATCHED LIMB IMITATION IN FAMS USERS**

### **Introduction**

Work from the previous chapter demonstrated that the action encoding parietofrontal network, which is crucial in planning and executing motor tasks, is less active in prosthesis users who imitate movements of intact actors (mismatched limb) versus prosthesis users (matched limb). Based on the EMG results (Table 4.2), it was proposed that mismatched limb training could have behavioral consequences during development of motor patterns in prosthesis users during therapist-led training with intact hands. The goal of this chapter was to identify behavioral effects of matched versus mismatched limb action imitation in naïve users of prostheses. Intact subjects donned a FAMS to simulate the wrist and forearm movement that transradial amputees experience. While electrogoniometry (ELGON) was recorded, subjects observed and imitated demonstrations of a skillful motor task performed by either an intact actor or FAMS user. The hypothesis stated that FAMS users would elicit less motion variability when performing matched versus mismatched imitation. These results would suggest a behavioral advantage to matched imitation when adapting to a prosthetic device, as it would yield more consistent movements with lower variability. This work has important implications on how prosthesis operation is conveyed to amputees during their initial training. Customary prosthetic rehabilitation with intact therapists involves mismatched

limb imitation that may exacerbate challenges in adapting to new motor patterns demanded by prosthesis use.

## **Materials and Methods**

### **Subjects**

Twenty right-handed intact subjects were recruited for this study (10 female, mean age =  $24.1 \pm 5.6$  years, range: 18-37 years). The Edinburgh Handedness Inventory (Oldfield 1971) was used to confirm handedness. Signed informed consent was acquired from all subjects according to the procedures set forth by the Institutional Review Board at The Georgia Institute of Technology.

### **Experimental Setup**

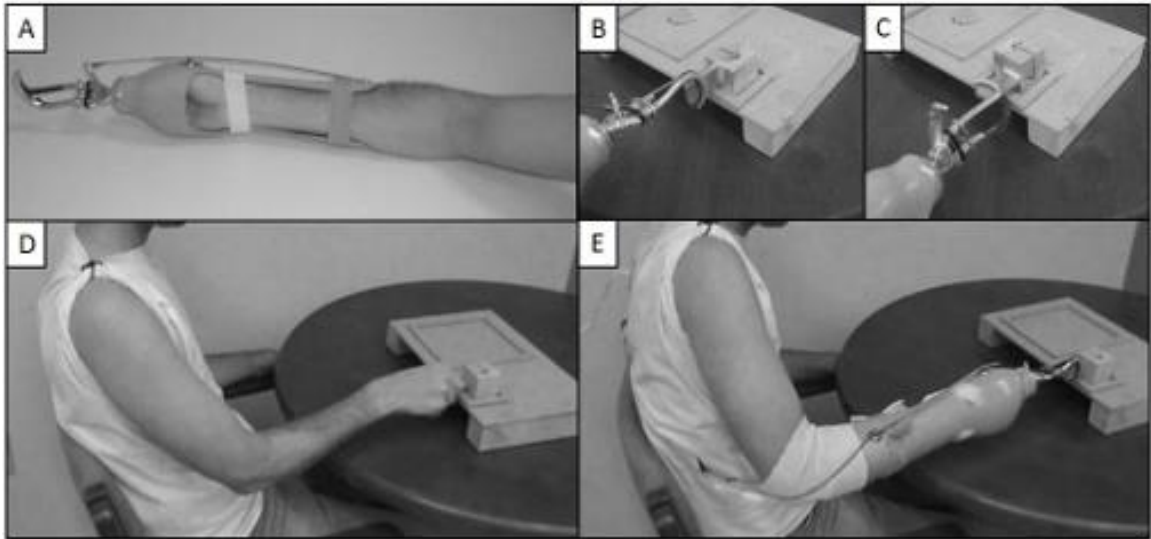
The right arm of each subject was fitted with three twin-axis goniometers and one single-axis torsionmeter (models SG110/150 and Q110/Q150, respectively, Biometrics Ltd, Newport, UK) that were connected to an 8-channel MyoSystem data collection system (model 1400L, Noraxon, Scottsdale, AZ, USA). Data was sampled with 1 kHz frequency and 12 bit resolution. There were four kinematic degrees of freedom in the arm that were of interest in this study: elbow flexion/extension (EFE), shoulder abduction/adduction (SAA), horizontal shoulder flexion/extension (SFE) and forearm supination/pronation (FRO). All sensors were applied using double-sided tape at the sensor-skin boundary and single-sided tape over and around the sensor. In preparation for the sensor placement, subjects sat comfortably with an upright posture, right arm abducted to  $90^\circ$ , elbow fully extended, and forearm supinated. Sensors were applied using guidelines provided by the manufacturer's user manual and previous studies in

upper extremity kinematics (Chao et al. 1980; Anglin and Wyss 2000; Hansson et al. 2004; Wise et al. 2004; Magermans et al. 2005; Biometrics 2010).

For EFE, the distal endblock of the goniometer was placed along the medial midline of the forearm, with long axes of the endblock and radius aligned. The proximal endblock was placed along the medial midline of the upper arm, with the long axes of the endblock and humerus aligned. The endblocks were positioned such that the center of the goniometer was directly over the medial epicondyle of the humerus. For SAA and SFE, the distal endblock of the goniometer was placed along the lateral midline of the upper arm, with the long axes of the endblock and humerus aligned. The proximal endblock was placed over the acromion, in line with the distal endblock and perpendicular to the midaxillary line of the thorax. The endblocks were positioned such that the center of the goniometer was directly over the greater tubercle of the humerus. For FRO, the torsionmeter was placed along the ventral midline of the forearm aligned with the long axis of the radius, with distal and proximal endblocks on the distal and proximal ends of the forearm, respectively. The distal endblock was placed approximately 1 cm from the ulnar and radial styloids.

Once the sensors were in place, all wires were taped to the arm and 1-3 layers of stockinette were donned to minimize movement related artifact. Next, each subject was fitted with a specially adapted FAMS socket that accommodates an intact subject's entire forearm and hand (Figure 5.1A). The device is designed to simulate the altered degrees of freedom in the wrist and forearm that a person with transradial amputation would experience after the loss or reduction of those joints. All subjects were naïve to the use of this device prior to the experiment. To ensure the best fit and highest comfort level for

each subject, additional foam padding was inserted between the skin and socket as needed. Once fitted with the FAMS, Velcro straps were used to tighten and secure the device. At the distal end of the socket was a commonly used hook-style terminal device (Model 5XA, Hosmer, Campbell, CA, USA) that was actuated via a body-powered harness. The mode of operation is similar to that which a person with transradial amputation using a prosthesis would experience. However, for the purposes of this study, no active prehension of the terminal device was required.



**Figure 5.1:** FAMS with Hosmer Model 5XA Hook terminal device (A), workspace board and block used for motor task in starting position (B) and rotated 90° clockwise (C), screenshots of intact (D) and FAMS (E) video demonstrations observed by subjects.

### Experimental Task

Subjects placed their elbow in a fixed location and rested their arm on a table within a fixed perimeter. A workspace board (Figure 5.1B,C) was then positioned on the table in front of the subject such that the midline of the board was aligned with the

vertical midline of the torso. The distance between the subject and the board was chosen such that the center of the workspace aligned with a fixed marker on the terminal device. In order to minimize the effect of compensatory trunk movements, subjects were seated in a fixed-height chair and brought close enough to a fixed-height table such that their torsos were confined by the edge of the table. On the table in front of each subject was a computer screen that was used to display a video demonstration of a motor task performed by either an intact actor or FAMS user. The motor task observed in both cases was adapted from the SHAP (Light et al. 2002).

The task involves: 1) placement of the wooden cube within the square target area (Position 1, Figure 5.1B), 2) lifting the cube, rotating 90° clockwise, placement back into target area (Position 2, Figure 5.1C), and 3) lifting the cube, rotating 90° counterclockwise, placement back into target area (Position 1, Figure 5.1B). The block (4.5 cm on each side) must be confined within the square target area (5.5 cm on each side) in both position 1 and position 2. Thus, it is comprised of two principal components: a rotation that permits the flipping of the block and a translation to control the end effector such that the block does not leave the workspace board target area. This task is a surrogate for the functionally relevant task of turning a key in a lock. We selected this as the model functional task as it represents a task that can be particularly difficult after transradial amputation. For intact individuals, this task configuration typically involves significant forearm pronation/supination and, to a lesser degree, wrist flexion/extension and wrist abduction/adduction. Each of these degrees of freedom are eliminated or severely limited by the FAMS. Thus, in order for FAMS users to imitate

the observed task, they adapt alternative control strategies in the remaining degrees of freedom; likely involving modified joint behavior in the elbow and shoulder.

Subjects viewed 30 s videos that contained ten repetitions of the motor task with the explicit instructions to remain motionless in a resting position. Subjects observed demonstrations performed by the intact actor (“mismatched limb”,  $n=10$ , Figure 5.1D) or by the actor using the FAMS (“matched limb”,  $n=10$ , Figure 5.1E). After the presentation of each video, subjects were explicitly instructed to “imitate the movement seen in the video as quickly and as accurately as possible” for a total of ten continuous repetitions. In order for the movements to be as natural as possible, no attempt was made to control the speed or pace of their movement repetitions. This pairing of observation followed by imitation was repeated 20 times; thus totaling 10 minutes of focused action observation and 200 movements over approximately 10 minutes of action imitation.

### **Data Analysis**

Kinematics from the four degrees of freedom of interest were obtained using ELGON and all further processing was performed using custom MATLAB software (version R2012a, The MathWorks Inc., Natick, MA, USA). All data were lowpass filtered backwards and forwards at 6 Hz with a fourth-order Butterworth filter. Data were then manually inspected on a subject level to identify the beginning and ending of each of the individual movements. Each instance of peak shoulder abduction was chosen to mark the beginning of each movement cycle, while the next instance was chosen as the end of that movement cycle. Behaviorally, these time points correspond to the transitions between counterclockwise and clockwise rotations in the block rotation task. The first instance of peak shoulder abduction served as the reference angle for the joint angle data.

All reported displacements in this study are relative to this reference position. Within each group of ten movements, the middle 8 were selected to eliminate movements related to the transport of the limb between the resting position and the workspace board. All angular displacement data were time normalized to percentage of the movement cycle. These 8 movements were averaged together into a representative movement for that particular movement group. The coefficient of variation (CV) for each of the 20 movement groups was calculated according to  $CV(\%) = \sigma(\%)/\mu(\%)$ ; where  $\sigma(\%)$  and  $\mu(\%)$  are the angular displacement standard deviation and mean as functions of percent movement cycle, respectively. This process was repeated on a subject level for each of the 20 groups of movements in the recording session. Additionally, for each of these 20 representative movements, the average CV was computed over the length of the entire movement cycle. Angular velocity was also computed for each of these 20 representative movements by numerically differentiating the averaged displacement data using the backward difference method.

In order to capture the dynamic behavior of each joint throughout the movement cycle, phase-plane analysis was performed. Angular displacement and velocity data were normalized to their respective minimum and maximum values, which resulted in values on the scale of -1 to 1, thus mitigating amplitude effects and differences in dimensionality (Lamoth et al. 2002; Davids et al. 2006). Phase-plane portraits were constructed by plotting angular velocity versus angular displacement, and then phase angle was calculated at each instance of time according to  $\varphi_i(t) = \tan^{-1}(\omega_i(t)/\theta_i(t))$ ; where  $\omega$  and  $\theta$  are normalized angular velocity and normalized angular displacement, respectively. Phase angles  $\varphi_{1:4}$  were calculated in the range of -180 to 180° for degrees of freedom

EFE, SAA, SFE, FRO, respectively. For plotting purposes, the absolute value of phase angle was computed; as  $-180^{\circ}$  and  $180^{\circ}$  represent the same point in the phase plane. The interjoint coordination profile was quantified by calculating CRP according to  $\theta_{CRP} = \varphi_2 - \varphi_1$ . Continuous relative phase (CRP) was calculated in the range of  $-360$  to  $360^{\circ}$  and then converted to the range of  $0$  to  $180^{\circ}$  to remove discontinuities due to phase wrapping (Kurz and Stergiou 2002; Lamothe et al. 2002; Davids et al. 2006). The three possible states of coordination are synchrony of two actions ( $0^{\circ} < CRP < 30^{\circ}$ ), asynchrony of two actions ( $150^{\circ} < CRP < 180^{\circ}$ ), and an intermediate phase relationship between the two actions ( $30^{\circ} < CRP < 150^{\circ}$ ) (Diedrich and Warren 1995; Seifert et al. 2010).

### **Statistical Design**

For statistical analysis, time series data were divided and averaged into 8 contiguous time windows, each representing 12.5% of the complete movement cycle. Due to the symmetric nature of the task, this selection of time windows allowed for each to capture distinct phases of the movement profile. A 3-way factorial ANOVA was performed with video (mismatched limb, matched limb), trial (1-20), and time window (1-8) as factors. Subsequent post hoc t-tests were performed, with significance set at  $p < 0.05$  using Bonferroni correction. All statistical tests were conducted using SPSS Statistics software (version 19, The IBM Corporation, Armonk, NY, USA).

## **Results**

### **Movement Angular Displacement**

Several degrees of freedom are eliminated or severely limited by the FAMS. Thus, in order for FAMS users to imitate the observed task, they adapt alternative control



strategies in the remaining degrees of freedom. Figure 5.2A-D shows the angular displacements at each degree of freedom during the task performances featured in the video demonstrations displayed to study participants. The intact performance featured extensive forearm supination/pronation that was greatly reduced once donning the FAMS (Figure 5.2D). In response, the rotational aspect of flipping the block is instead performed by increased adduction/abduction in the shoulder (Figure 5.2B). Additionally, the forward and backward translational aspects of the task are accomplished by a combination of increased elbow and shoulder flexion/extension (Figure 5.2A,C). A notable difference between the demonstrations is that the intact motor pattern consists of elbow flexion followed by extension, while the FAMS motor pattern is reversed, with extension followed by flexion (Figure 5.2A).

#### Elbow Flexion/Extension (EFE)

ANOVA of EFE angular displacement between matched limb and mismatched limb revealed a main effect of video,  $F(1, 2080) = 569, p < .001$ . There was also an interaction between video and time window,  $F(7, 2080) = 35.4, p < .001$ . Post-hoc analyses indicated differences during 0-87.5% of the movement cycle, all comparisons  $F(1, 2080) \geq 4.11, p \leq .043$  (Figure 5.2E). Behaviorally, the limb matched group demonstrated a similar pattern of EFE extension followed by flexion as performed by the FAMS actor in the observed video. The limb mismatched group demonstrated the same pattern of EFE flexion followed by extension as performed by the intact actor in the observed video (Figure 5.2A).

#### Shoulder Abduction/Adduction (SAA)

An ANOVA performed on SAA angular displacement revealed a main effect of video,  $F(1, 2080) = 20.0, p < .001$ . An interaction effect was seen between video and time window,  $F(7, 2080) = 2.34, p = .022$ . Post-hoc analyses indicated differences during 25-75% of the movement cycle, all comparisons  $F(1, 2080) \geq 5.45, p \leq .020$  (Figure 5.2F). Behaviorally, the matched limb group showed less shoulder adduction and abduction compared to the mismatched group. Unique to this degree of freedom, a main effect of trial was observed,  $F(19, 2080) = 3.72, p < .001$ . Across both groups, the SAA range of motion decreased over the length of the experiment such that average SAA angular displacement for trial numbers 19 (mean=-2.35±0.23) and 20 (mean=-2.31±0.23) was significantly less than that of trial numbers 2 (mean=-3.68±0.23), 3 (mean=-3.65±0.23), and 7 (mean=-3.51±0.23).

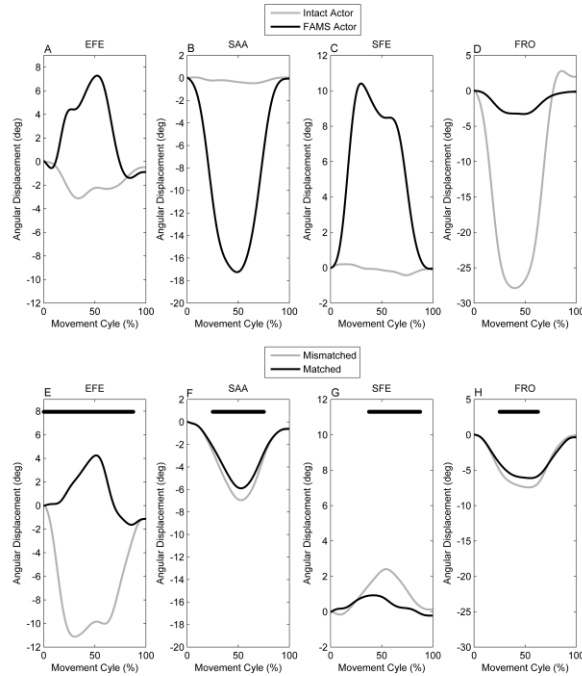
#### Shoulder Flexion/Extension (SFE)

The results of an ANOVA on SFE angular displacement revealed a main effect of video,  $F(1, 2080) = 43.8, p < .001$ . An interaction effect between video and time window was seen,  $F(7, 2080) = 7.01, p = .022$ . Post-hoc analyses indicated differences during 37.5-87.5% of the movement cycle, all comparisons  $F(1, 2080) \geq 4.62, p \leq .032$  (Figure 5.2G). Behaviorally, the matched limb group showed less shoulder flexion/extension compared to the mismatched group.

#### Forearm Supination/Pronation (FRO)

ANOVA results on FRO angular displacement revealed a main effect of video,  $F(1, 2080) = 20.2, p < .001$ . An interaction was seen between video and time window,  $F(7, 2080) = 5.18, p < .001$ . Post-hoc analyses indicated differences during 25-62.5% of the movement cycle, all comparisons  $F(1, 2080) \geq 15.0, p \leq .001$  (Figure 5.2H).

Behaviorally, the matched limb group showed less forearm supination/pronation compared to the mismatched group.



**Figure 5.2:** Angular displacements of intact and FAMS actor for elbow flexion/extension (EFE) (A), shoulder abduction/adduction (SAA) (B), shoulder flexion/extension (SFE) (C), and forearm supination/pronation (FRO) (D) and of matched and mismatched imitation groups in EFE (E), SAA (F), SFE (G), FRO (H). Black markers indicate movement cycle segments during which group differences in matched versus mismatched imitation displacement were found below the  $p < 0.05$  statistical threshold.

## CV

Average CV over the entire movement cycle (Figure 5.3A-D) and CV as a function of % movement cycle (Figure 5.3E-H) were calculated to quantify progressive changes in movement variability.

### Elbow Flexion/Extension (EFE)

ANOVA of EFE CV between matched limb and mismatched limb revealed a main effect of video,  $F(1, 2080) = 65.0, p < .001$ . The matched limb group performed movements with higher average CV (mean=0.027±4.74e-4) than the mismatched group (mean=0.022±4.44e-4, Figure 5.3A). There was an interaction effect between video and time window,  $F(7, 2080) = 4.19, p < .001$ . Post-hoc analyses indicated that matched limb CV was higher than that of mismatched limb during 12.5-37.5% and 50-87.5% of the movement cycle, all comparisons  $F(1, 2080) \geq 4.80, p \leq .029$  (Figure 5.3E).

### Shoulder Abduction/Adduction (SAA)

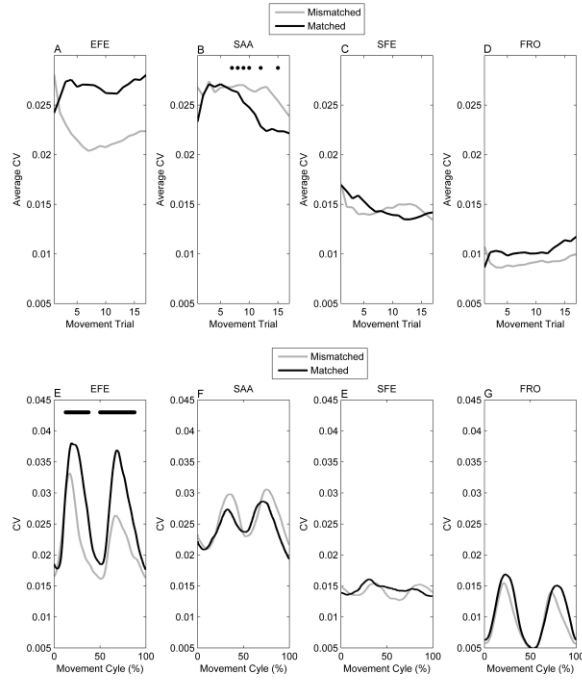
An ANOVA performed on SAA CV revealed a main effect of trial,  $F(19, 2080) = 3.21, p < .001$ . Unique to this degree of freedom, there was an interaction effect between video and trial,  $F(19, 2080) = 2.36, p = .001$ . Post-hoc analyses indicated that matched limb summed CV was lower than that of mismatched limb at trial numbers 7, 8, 9, 10, 12, and 15, all comparisons  $F(1, 2080) \geq 4.30, p \leq .038$  (Figure 5.3B). No main effect of video or interaction effect of video and time window was found in SAA CV (Figure 5.3F).

### Shoulder Flexion/Extension (SFE)

The results of an ANOVA on SFE CV showed no main effects of video/trial or interaction effect of video and time window/video and trial (Figure 5.3C,G).

### Forearm Supination/Pronation (FRO)

ANOVA results on FRO CV revealed a main effect of video,  $F(1, 2080) = 11.1, p < .001$  and a main effect of trial,  $F(19, 2080) = 1.756, p = .023$ . The matched limb group performed movements with higher average CV (mean= $0.011 \pm 2.88e-4$ ) than the mismatched group (mean= $0.009 \pm 2.69e-4$ , Figure 5.3D). No interaction effect of video and time window or video and trial were found in FRO CV (Figure 5.3H).



**Figure 5.3:** Average CV for matched and mismatched imitation groups across all movement trials for EFE (A), SAA (B), SFE (C), and FRO (D). CV of matched and mismatched imitation groups across movement cycle in EFE (E), SAA (F), SFE (G), and FRO (H). Black markers indicate movement cycle segments or movement trials during which group differences in matched versus mismatched imitation CV were found below the  $p < 0.05$  statistical threshold.

## **Movement Phase Angle and CRP**

Phase angle and CRP were calculated to quantify the dynamics of each degree of freedom and the interjoint coordination between SAA and EFE for demonstration actors (Figure 5.4A-D, Figure 5.5A-B) and experimental groups (Figure 5.4E-H, Figure 5.5C-D).

### Elbow Flexion/Extension (EFE)

ANOVA of EFE phase angle between matched limb and mismatched limb revealed a main effect of video,  $F(1, 2080) = 3.98, p = .046$ . There was an interaction effect between video and time window,  $F(7, 2080) = 95.6, p < .001$ . Post-hoc analyses indicated phase angle differences during 0-100% of the movement cycle, all comparisons  $F(1, 2080) \geq 9.10, p \leq .003$  (Figure 5.4E). Behaviorally, the limb matched group demonstrated comparable EFE dynamics compared to those performed by the FAMS actor in the observed video (Figure 5.4A,E). Similarly, the limb mismatched group also demonstrated similar EFE dynamics compared to those performed by the intact actor in the observed video (Figure 5.4A,E).

### Shoulder Abduction/Adduction (SAA)

An ANOVA performed on SAA phase angle did not reveal a main effect of video or an interaction effect of video and time window (Figure 5.4F).

### Shoulder Flexion/Extension (SFE)

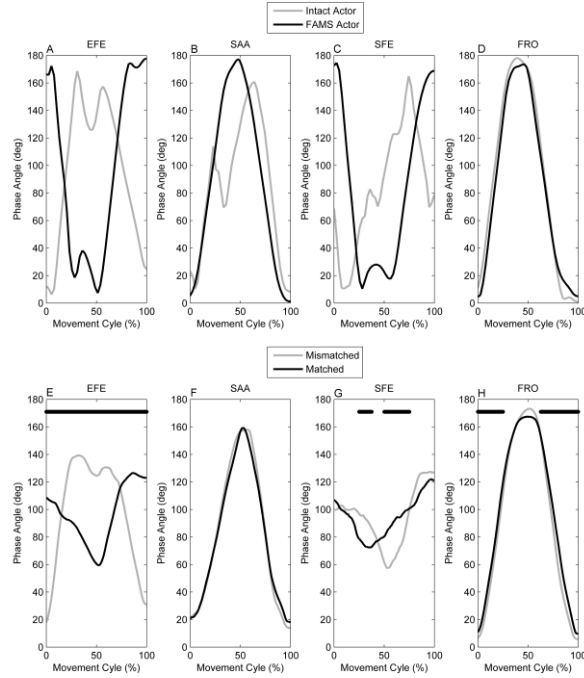
The results of an ANOVA on SFE phase angle did not reveal a main effect of video,  $F(1, 2080) = .001, p = .977$ , but did reveal an interaction effect of video and time window,  $F(1, 2080) = 5.74, p < .001$ . Post-hoc analyses indicated phase angle differences



during 25-37.5% and 50-75% of the movement cycle, all comparisons  $F(1, 2080) \geq 5.82$ ,  $p \leq .016$  (Figure 5.4G).

#### Forearm Supination/Pronation (FRO)

ANOVA results on FRO phase angle revealed a main effect of video,  $F(1, 2080) = 25.6$ ,  $p < .001$ . There was an interaction effect between video and time window,  $F(7, 2080) = 4.29$ ,  $p < .001$ . Post-hoc analyses indicated phase angle differences during 0-15% and 62.5-100% of the movement cycle, all comparisons  $F(1, 2080) \geq 6.24$ ,  $p \leq .013$  (Figure 5.4H).

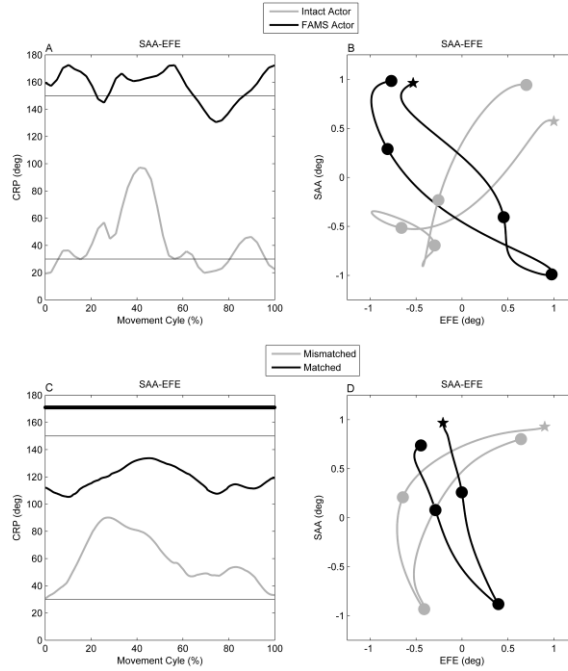


**Figure 5.4:** Phase angle of intact and FAMS actor for EFE (A), SAA (B), SFE (C), and FRO (D), and of matched and mismatched imitation groups in EFE (E), SAA (F), SFE (G), FRO (H). Black markers indicate movement cycle segments during which group differences in matched versus mismatched imitation phase angle were found below the  $p < 0.05$  statistical threshold.

## **SAA-EFE CRP**

Due to the observation of significant motor behavioral effects of video on SAA and EFE angular displacement and CV, an ANOVA was performed on SAA-EFE CRP. This analysis between matched limb and mismatched limb revealed a main effect of video,  $F(1, 2080) = 117, p < .001$  and an interaction effect between video and time window,  $F(7, 2080) = 5.82, p < .001$ . Post-hoc analyses indicated CRP differences during 0-100% of the movement cycle, all comparisons  $F(1, 2080) \geq 9.95, p \leq .002$  (Figure 5.5C). Both matched and mismatched limb SAA-EFE coordination profiles show sustained periods of intermediate phase in the  $30^\circ < \text{CRP} < 150^\circ$  range. The range of matched limb imitation CRP is near the antiphase range ( $150^\circ < \text{CRP} < 180^\circ$ ), which indicates a behavioral motor pattern of elbow extension paired with shoulder adduction followed by elbow flexion paired with shoulder abduction. Contrastingly, the range of mismatched limb is near the synchronous phase range ( $0^\circ < \text{CRP} < 30^\circ$ ), which indicates the pairing of elbow flexion and shoulder adduction followed by elbow extension paired with shoulder abduction. Behavioral differences between these interjoint coordination patterns are displayed as normalized angle-angle plots in Figure 5.5D. Both groups, but particularly the matched limb group, demonstrate turning-point coordination for the majority of the movement cycle as indicated by the approximately linear slope of the angle-angle plots. Corroborating the CRP data, the predominantly negative slope of the matched limb group and predominantly positive slope of mismatched limb group indicate approximately decoupled and coupled coordination, respectively. Importantly, the SAA-EFE CRP and angle-angle plot differences described above are also found between the FAMS actor and intact actor performances featured in the observed videos (Figure 5.5A

versus 5C, Figure 5.5B versus 5D). Namely, the FAMS actor and matched imitation group display mostly antiphase coordination, while the intact actor and mismatched imitation group display principally in-phase coordination.



**Figure 5.5:** SAA-EFE CRP (A) and normalized angle-angle plots (B) for intact and FAMS actor demonstrations. SAA-EFE CRP (C) and normalized angle-angle plots (D) for matched and mismatched imitation groups. For reference in the angle-angle plots, stars mark the beginning of each movement cycle, which all progress in the counterclockwise direction. Consecutive circles mark 25%, 50%, 75% and 100% of the movement cycles. Horizontal line at  $30^\circ$  marks the threshold between in-phase (below) and intermediate phase coordination. Black markers indicate movement cycle segments during which group differences in matched versus mismatched imitation CRP were found below the  $p < 0.05$  statistical threshold.

## **Movement Duration**

The results of an ANOVA on movement duration between matched limb and mismatched limb revealed a main effect of video,  $F(1, 260) = 19.8, p < .001$ . The matched limb group performed movements slower (mean=2427±59.0ms) than the mismatched group (mean=2067±55.2ms). No main effect of trial or interaction effect of video and trial was observed.

## **Discussion**

The goal of the current chapter was to further identify the behavioral effects of matched limb versus mismatched limb observation and imitation in naïve users of prosthetic devices. Intact subjects were recruited and fitted with the FAMS device to simulate the altered degrees of freedom in the wrist and forearm that a person with transradial amputation would experience after the loss or reduction of those joints. Subjects viewed video demonstrations of a motor task being performed by either an intact actor (mismatched limb condition) or a FAMS user (matched limb condition). After observation, subjects were told to imitate the movement seen in the video with the newly fitted FAMS device. During the course of the experiment, matched limb imitation resulted in a greater decrease in SAA movement variability compared to mismatched limb imitation. This result suggests a behavioral advantage to matched imitation when adapting to the FAMS, as it yielded more consistent and prototypical SAA movements during the latter half of the experiment. Further, FAMS users in the matched limb group appear to adapt the novel EFE and SAA movement dynamics of the FAMS actor, while FAMS users in the mismatched limb group appear to continue using the EFE and SAA movement dynamics of the intact actor. Within the movement cycle, matched limb

imitation resulted in greater variability in EFE, the degree of freedom that required the largest behavioral shift in order to successfully imitate the observed movement. Together, these results suggest that video demonstration type can affect the imitation kinematics, dynamics, and variability in intact users of a novel prosthetic device. This finding has important implications on how prosthetic device operation is conveyed to persons with amputation during their initial rehabilitation and prosthesis training.

There were several limitations in the current chapter. As described above, a main effect of video on movement duration was found; with matched limb imitation showing longer duration than mismatched limb imitation. However, despite a trend of decreasing movement duration throughout the experiment, there was no main effect of trial or interaction effect of video X trial on movement duration. It is suggested that despite the novelty of using the FAMS, the motor task itself was not difficult enough to elicit the documented pattern of initially high movement duration, followed by a decrease as a function of practice (Flament et al. 1999; Smeets 2000). Nonetheless, several other calculated metrics previously shown to be accurate measures of motor adaptation exhibited main effects of trial and interaction effects of video X trial. Future studies may involve more difficult motor tasks, ADLs, and longitudinal assessments to illustrate behavioral effects.

### **Effect of Limb Demonstration Type on Adaptation to the FAMS**

For intact individuals, the rotational component of the task relies heavily on forearm supination and pronation, the degree of freedom most limited by use of the FAMS (Figure 5.2D). In the case of the FAMS users, this reduced rotational capability is principally compensated for by increased shoulder adduction and abduction (Figure

5.2B). Therefore, changes in performance in SAA are likely driven by the adaptation to the FAMS device itself, a task feature common to both experimental groups. Despite numerical differences in displacement profiles in the second and third quarters of the movement cycle, SAA movement profiles were qualitatively similar between the groups, showing a pattern of adduction followed by abduction. However, over the length of the experiment, matched limb imitation resulted in a greater decrease in movement variability compared to mismatched limb imitation. In alignment with the hypothesis, this result suggests a behavioral advantage to matched imitation, as it yielded more consistent and prototypical movements during the latter half of the experiment. Movements with lower variability have been associated with better technique (Payton et al. 2007; Winter 2009). This result suggests that matched limb imitation more effectively facilitates the formation of the new SAA movement strategy required to successfully perform the task with the kinematic restraints of the FAMS device.

It has been demonstrated that the acquisition of novel motor skill is accompanied with changes in coordination and control of individual joints and the coupling between joints (Vereijken et al. 1992). The underlying drive for these changes has been cited as the automatic management of degrees of freedom in order to, at least initially, reduce the complexity of movement required to accomplish the task. This process can involve the reduction or “freezing” of specific degrees of freedom while others are free to utilize the available range of motion. Additionally, multiple degrees of freedom may be coupled together to create a single virtual degree of freedom (Calvin et al. 2004; Hodges et al. 2005; Konczak et al. 2009). Both of these phenomena result in a decrease in the number of individual degrees of freedom that must be controlled at one time, which shifts the



burden of control to the remaining degrees of freedom. Once adequate control of the “free” degrees of freedom is obtained, the modified degrees of freedom can be released and incorporated into a more sophisticated control strategy (Bernshteĭn 1967; Hodges et al. 2005). Practically, this reversal results in increased range of motion for the frozen degrees of freedom and the transition from in-phase coordination to intermediate phase coordination between the previously coupled joints. Results show that mismatched limb SAA-EFE coordination is nearly in-phase, perhaps reflecting the continued reduction in degrees of freedom associated with early adaptation to a novel motor task. Contrastingly, matched limb imitation exhibited a nearly intermediate phase relationship and a greater CRP value in SAA-EFE during the majority of the movement cycle. This result suggests the unfreezing of degrees of freedom typically associated with successful motor task adaptation.

In intact individuals and FAMS users alike, the translational component of the task relies heavily on EFE and SFE, degrees of freedom not directly constrained by use of the FAMS. It is in these DOFs where the largest behavioral main effects of the video demonstration type were found. In the case of EFE, a major behavioral change was evident; with the matched limb group exhibiting a pattern of extension followed by flexion, while the mismatched limb group showed the opposite pattern of flexion followed by extension. Correspondingly, the EFE phase angle and SAA-EFE CRP patterns of each group demonstrate opposite patterns of dynamic behavior. Importantly, these divergent behavioral patterns matched the same behavioral differences observed in the video demonstrations of intact or FAMS actors. Namely, FAMS users in the matched limb group appear to adapt the novel movement pattern of the FAMS actor, while FAMS

users in the mismatched limb group appear to continue using the movement pattern of the intact actor.

Contrary to the hypothesis, the EFE behavior in the matched limb condition was accompanied by greater variability throughout the majority of the movement cycle compared to the mismatched limb condition. Previous work has shown that during acquisition of a skill requiring novel coordinative strategies, changes in learned movement patterns can be accompanied with the destabilizing of associated degrees of freedom (Calvin et al. 2004). Thus, the change in coordination pattern may have resulted in greater EFE variability throughout the movement cycle for the matched limb condition. This alteration in movement pattern may also explain why matched limb imitation movements were generally longer in duration than those of the mismatched limb group over the course of the experiment. These results suggest that video demonstration type can affect task imitation performance, variability, and duration.

Previous work has shown that during acquisition of a skill requiring novel coordinative strategies, changes in learned movement patterns can be accompanied with the stabilizing and destabilizing of associated degrees of freedom (Calvin et al. 2004). This process is thought to provide flexibility and stability to the limb system as changes in coordination are manifested in order to accomplish task-specific actions (Buchanan and Kelso 1999; Fink et al. 2000). In the current study, the task-specific action involved imitating the movements observed in the video demonstrations. In order for the matched limb imitation group to successfully do so, a major behavioral shift in EFE was required. It is suggested that, in the case of matched limb imitation, the original coordinative strategy for EFE was destabilized in order to allow for the imitation and adaptation of the

observed movement pattern with the FAMS. This coordination destabilization may have resulted in greater EFE variability throughout the movement cycle for the matched limb condition. This EFE destabilization process and the corresponding change in movement pattern may also explain why matched limb imitation movements were generally longer in duration than those of the mismatched limb group over the course of the experiment. Increased movement duration (Smeets 2000) and variability (Flament et al. 1999; Kempf et al. 2001) have been attributed to inexperience with a novel motor task.

The finding that movement variability of rotational (SAA) and translational (EFE) degrees of freedom are apparently managed differently in the matched limb condition aligns well with established work. While the standard framework for novel motor task learning was originally described by a pattern of changes in variability progressing from proximal to distal joints, previous work has shown that this process does not necessarily follow a stereotypical pattern (McDonald et al. 1989). For example, it has been proposed that this process can be influenced by factors such as task constraints (Carson and Riek 1998; Carson and Riek 2001), informational context (Calvin et al. 2004), and degree of practice (Hodges et al. 2005). Further, it has been shown that within a particular task, motor skill acquisition behavior can vary across joints (Hodges et al. 2005), degrees of freedom (Konczak et al. 2009), and motion planes (Calvin et al. 2004).

### **Neural Basis for Performance Differences**

Prior work has shown that specific areas within the premotor, motor, and parietal cortices are activated when planning, executing and observing motor tasks (Cattaneo and Rizzolatti 2009). The degree to which this parietofrontal action encoding system is activated by motor task observation is described by the concept of motor resonance. It

has been proposed that observation of an action drives an internal replication of that action in the motor system of the observer in a somatotopic manner (Buccino et al. 2001). According to the direct-matching hypothesis, this process involves the transformation of observed actions onto the corresponding motor representations in the observer (Rizzolatti et al. 2001). Thus, activation of this parietofrontal network via motor resonance may provide a mechanism by which we can understand, learn, and imitate the actions of others from our own internal perspective (Rizzolatti and Sinigaglia 2010). Further characterizing this system, recent work has suggested that the parietofrontal action encoding network may be preferentially engaged by limb movements that are similar in appearance and kinematic capabilities to that of the viewer. Specifically, sensorimotor areas can be deactivated during observation of a human action that is robot-like or movement performed by a virtual robotic actor with human-like kinematics (Tai et al. 2004; Shimada 2010).

Chapter 4 showed that prosthesis users who observed and imitated actions performed by matched prosthesis users showed greater left parietofrontal activation compared to those that imitated demonstrations performed by intact actors (Cusack et al. 2012). This finding suggests that prosthesis users can engage the typical left hemispheric action encoding activity when they imitate a limb state that matches their own. Based on the motor resonance conceptual framework and our work in action observation and imitation in prosthesis users, it is proposed that matched limb imitation in the current study engages the parietofrontal system to a greater degree as a result of enhanced motor resonance between the subject and actor. As has been demonstrated in intact subjects previously, engagement of the parietofrontal network is important for the planning and

execution of tool-use movement and imitation (Goldenberg et al. 2007; Hermsdorfer et al. 2007; Cattaneo and Rizzolatti 2009; Tsuda et al. 2009; Rizzolatti and Sinigaglia 2010). Additionally, enhanced motor resonance can also account for activation of the corticospinal pathways and task-specific muscles during action observation (Strafella and Paus 2000; Funase et al. 2007; Alaerts et al. 2009). It is suggested that in the case of the matched limb imitation group, observing the movements performed by the FAMS actor better facilitated the formation of the new movement strategy compared to the mismatched limb condition. Thus, engaging the parietofrontal action encoding system may underlie the beneficial performance effects reported in matched limb FAMS users in the current study.

In Chapter 4, mismatched imitation in prosthesis users resulted in increased right parietal and occipital activity in addition to the typical parietofrontal activity during movement planning compared to matched limb imitation (Cusack et al. 2012). We argued that due to the mismatch of the subject's arm with that of the video demonstration, the planning phase could no longer proceed as normal. It is proposed that this functional incongruity results in the increased demand of the task and thus, requires additional parietooccipital activity to facilitate visuospatial action encoding strategies (Buccino et al. 2004a). At the time, due to differential trends in muscle activation order, we suggested that the atypical engagement of the visuomotor system in prosthesis users may have behavioral and performance consequences as differential muscle recruitment patterns will alter movement kinematics. In the case of mismatched limb imitation in the current study, it is suggested that a decrease in motor resonance and functional congruity between the subject and actor results in lesser engagement of the parietofrontal network and greater

engagement of the parietooccipital network. The increased visuospatial demand of the mismatched limb imitation task may require additional parietooccipital activity to facilitate the task performance (Buccino et al. 2004a). This concept is supported by recent research showing that familiarity with a tool can influence activations in the parietofrontal areas in an action observation and imitation training paradigm. Namely, subjects who imitated video demonstrations of a familiar tool showed greater activations in the parietofrontal areas, compared to those who imitated an unfamiliar tool, which elicited greater activations in the parietooccipital areas (Mizelle et al. 2011). The proposed change of relative weighting between the two action encoding systems due to differing levels of exposure to the FAMS may explain the differences in movement variability and coordinative strategy observed in the current study.

## **Conclusion**

The results of the current chapter suggest that there are beneficial effects of matched limb observation and imitation on the performance of motor tasks in novel users of a prosthetic device. These findings have important clinical implications, as customary prosthetic rehabilitation in persons with amputations involves interaction with occupational therapists who are normally intact and able-bodied individuals themselves. This chapter contributes unique insights into the process of adapting to the functional constraints of a novel prosthetic limb and will be extended into a clinical population of persons with upper extremity amputation in the next chapter.

# **CHAPTER 6**

## **MOTOR PERFORMANCE BENEFITS OF MATCHED LIMB IMITATION IN PERSONS WITH AMPUTATION**

### **Introduction**

The previous chapter demonstrated that intact users of the FAMS who performed matched limb imitation showed a decrease in shoulder motion variability compared to those who performed mismatched limb imitation. The goal of the pilot work (n=4) in this chapter is to expand the investigation into a population of persons with upper extremity amputation and to identify behavioral effects of matched versus mismatched limb action. While electrogoniometry (ELGON) was recorded, subjects observed and imitated demonstrations of a skillful motor task performed by either an intact actor (mismatched limb) or prosthesis user (matched limb). As with the previous chapter, the hypothesis stated that matched limb imitation would elicit less motion variability when subjects performed the motor task with their prosthesis. These findings would suggest a behavioral advantage to matched imitation in persons with amputation and may suggest implications on how prosthesis operation is conveyed to persons with amputation.

### **Methods and Materials**

#### **Subjects**

Four right-handed persons with upper extremity amputation were recruited for this study (1 female, 3 male, mean age =  $41.0 \pm 15.2$  years, range: 25-61 years). The Edinburgh Handedness Inventory was used to confirm recalled original handedness prior

to amputation (Oldfield 1971). Signed informed consent was acquired from all subjects according to the procedures set forth by the Institutional Review Board at The Georgia Institute of Technology. Persons with amputation reported wearing their prosthetic devices an average of  $7.3 \pm 7.4$  hours/day. Average psychosocial adjustment of these subjects to their prostheses, as assessed by the TAPES survey (Gallagher and MacLachlan 2000; Desmond and MacLachlan 2005), was calculated to be  $52.3 \pm 4.8$  (on a scale from 14-70, with higher values indicating greater adjustment). Before being recruited into the protocol, all subjects were screened for the presence of any other neurologic factors, including (but not limited to) traumatic brain injury, stroke, or concussion. The presence of phantom limb syndrome/pain was an exclusion criterion for the amputee subjects. The amputee population was made up of persons who had lost their limb due to occupational and recreational accidents with no brain trauma. Demographic and clinically relevant information for the prosthesis users is presented in Table 6.1. Of the seven subjects that were originally recruited, three subjects were excluded for not complying with the experimental paradigm. This noncompliance was related to the high difficulty of the motor task and is discussed below.

**Table 6.1:** Demographic and clinically relevant information for the persons with amputation. MIS= mismatched limb imitation, MAT=matched limb imitation, Dom= original hand dominance, Amp=amputation, TRAU=traumatic, TR=transradial, PX=prosthetic device, Body=body powered, Myo=myoelectric, TD=terminal device, PAS=Psychosocial Adjustment Scale (on a scale from 14-70, with higher values indicating greater adjustment).

	Sex	Age (yrs)	Dom	Amp cause	Level	Amp side	Yrs since amp	Yrs since 1 <sup>st</sup> PX	Yrs with current PX	Power type	TD	PX use (hrs/day)	PAS
MIS_001	M	61	R	TRAU	TR	R	6.5	6.0	2.0	Body	Hook	3	51
MIS_002	F	25	R	TRAU	TR	R	1.0	0.8	0.8	Body	Hook	2	46
MAT_001	M	45	R	TRAU	TR	R	25.0	25.0	23.0	Body	Hook	18	56
MAT_002	M	35	R	TRAU	TR	R	3.1	2.9	0.4	Body	Hook	6	56
Mean $\pm$ SD	---	41.0 $\pm$ 15.2	---	---	---	---	8.9 $\pm$ 11.0	8.7 $\pm$ 11.1	6.6 $\pm$ 11.0	---	---	7.3 $\pm$ 7.4	52.3 $\pm$ 4.8



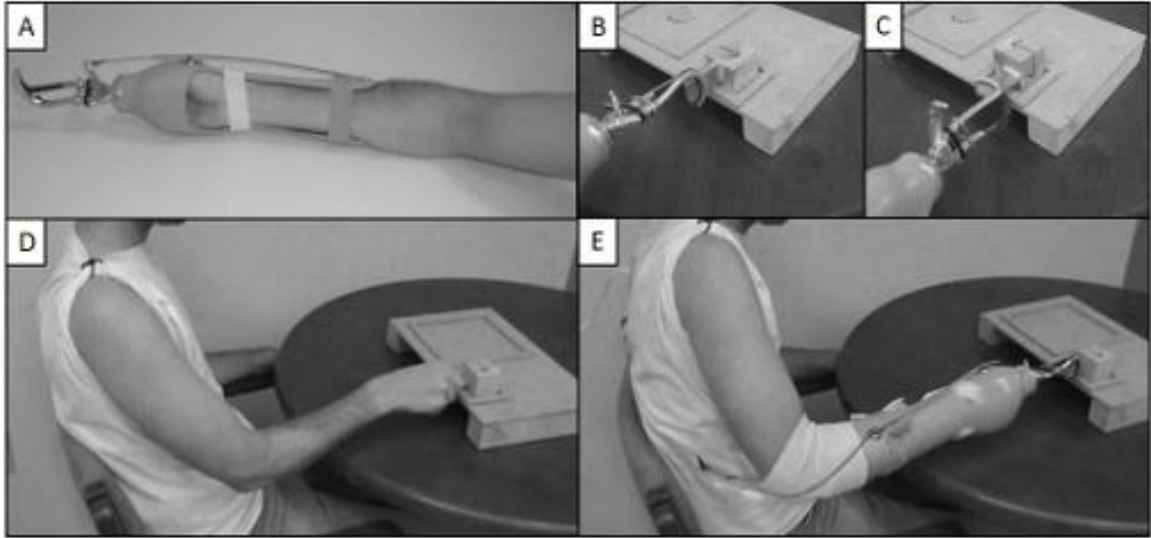
## **Experimental Setup**

The right arm of each subject was fitted with three twin-axis goniometers and one single-axis torsionmeter (models SG110/150 and Q110/Q150, respectively, Biometrics Ltd, Newport, UK) that were connected to an 8-channel MyoSystem data collection system (model 1400L, Noraxon, Scottsdale, AZ, USA). Data was sampled with 1 kHz frequency and 12 bit resolution. There were two physiological degrees of freedom in the arm that were of interest in this study: elbow flexion/extension (EFE) and shoulder abduction/adduction (SAA). Sensors were applied using guidelines provided by the manufacturer's user manual and previous studies in upper extremity kinematics (Chao et al. 1980; Anglin and Wyss 2000; Hansson et al. 2004; Wise et al. 2004; Magermans et al. 2005; Biometrics 2010).

## **Experimental Task**

Subjects placed their elbow in a fixed location and rested their arm on a table within a fixed perimeter. A workspace board (Figure 6.1) was then positioned on the table in front of the subject such that the midline of the board was aligned with the vertical midline of the torso. The distance between the subject and the board was chosen such that the center of the workspace aligned with a fixed marker on the terminal device. In order to minimize the effect of compensatory trunk movements, subjects were seated in a fixed-height chair and brought close enough to a fixed-height table such that their torsos were confined by the edge of the table. On the table in front of each subject was a computer screen that was used to display a video demonstration of a motor task performed by either an intact actor or FAMS user. The motor task observed in both cases

was adapted from the SHAP (Light et al. 2002). The task involved here is identical to that in Chapter 5 and its components are depicted in Figure 6.1 B,C.



**Figure 6.1:** Prosthesis with Hosmer Model 5XA Hook terminal device (A), workspace board and block used for motor task in starting position (B) and rotated 90° clockwise (C), screenshots of intact (D) and FAMS (E) video demonstrations observed by subjects.

Subjects viewed 30 s videos that contained ten repetitions of the motor task with the explicit instructions to remain motionless in a resting position. Subjects observed demonstrations performed by the intact actor (“mismatched limb”,  $n=2$ , Figure 6.1D) or by the actor using the FAMS (“matched limb”,  $n=2$ , Figure 6.1E). After the presentation of each video, subjects were explicitly instructed to “imitate the movement seen in the video as quickly and as accurately as possible” for a total of ten continuous repetitions. In order for the movements to be as natural as possible, no attempt was made to control the speed or pace of their movement repetitions. This pairing of observation followed by

imitation was repeated 20 times; thus totaling 10 minutes of focused action observation and 200 movements over approximately 10 minutes of action imitation.

### **Data Analysis**

Kinematics from the two degrees of freedom of interest were obtained using ELGON and all further processing was performed using custom MATLAB software (version R2012a, The MathWorks Inc., Natick, MA, USA). All data were lowpass filtered at 6 Hz with a fourth-order Butterworth filter and then manually inspected on a subject level to identify the beginning and ending of each of the individual movements. Each instance of minimum shoulder abduction was chosen to mark the beginning of each movement cycle, while the next instance was chosen as the end of that movement cycle. Behaviorally, these time points correspond to the transitions between counterclockwise and clockwise rotations in the block rotation task. The first instance of minimum shoulder abduction served as the reference position for the ELGON data. All reported displacements in this study are relative to this reference position.

Within each group of ten movements, the middle 8 were selected to eliminate movements related to the transport of the limb between the resting position and the workspace board. Average movement duration was calculated at each of the 20 movement groups. Decreased movement duration over consecutive movement trials has previously been shown to be an accurate measure for quantifying motor adaptation (Flament et al. 1999; Kempf et al. 2001; Smith et al. 2006).

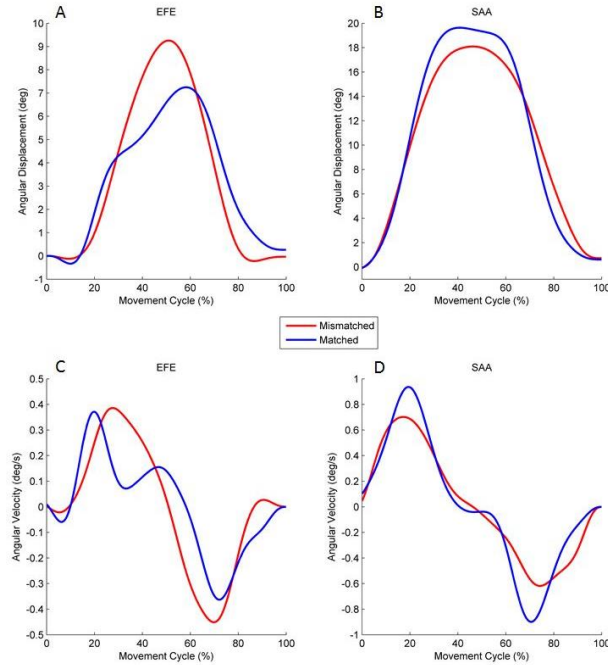
Next, angular displacement data were time normalized to percentage of the movement cycle. These 8 movements were averaged together into a representative movement for that particular movement group. The CV for each of the 20 movement

groups was calculated according to  $CV(\%) = \sigma(\%)/\mu(\%)$ ; where  $\sigma(\%)$  and  $\mu(\%)$  are the angular displacement standard deviation and mean as functions of percent movement cycle, respectively. This process was repeated on a subject level for each of the 20 groups of movements in the recording session. Additionally, for each of these 20 representative movements, the average CV was computed over the length of the entire movement cycle. Angular velocity was also computed for each of these 20 representative movements by numerically differentiating the averaged displacement data.

## **Results**

### **Movement Angular Displacement and Velocity**

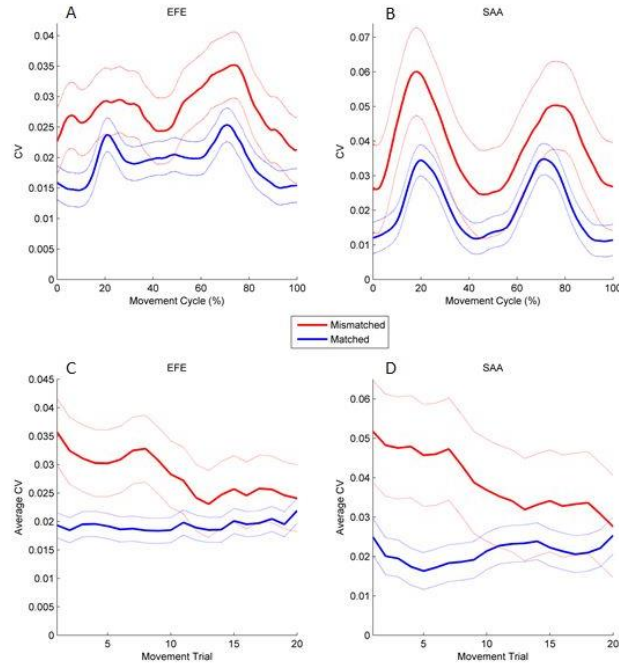
Average angular displacement (Figure 6.1 A,B) and velocity (Figure 6.1 D,C) over the entire movement cycle were measured to quantify the motor behavior of the limb matched and limb mismatched imitation groups. Comparison of average angular displacement and velocity profiles in EFE and SAA suggest that each group performed the motor task using qualitatively similar patterns of movement. Specifically, both groups demonstrate a pattern of elbow extension followed by flexion and shoulder abduction followed by adduction. Over the length of the entire experiment, both groups also exhibit qualitatively similar velocity profiles with comparable peaks in velocity.



**Figure 6.2:** Angular displacements and velocities of matched and mismatched imitation groups in EFE (A,C) and SAA (B,D), respectively.

## CV

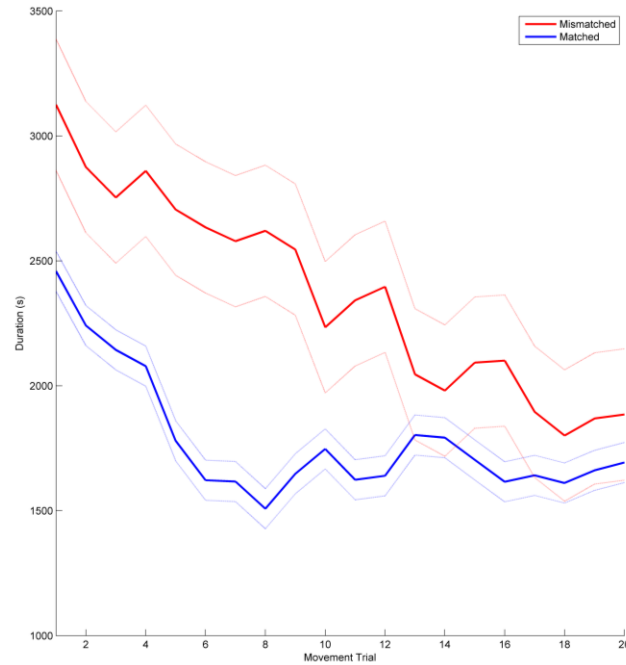
Average CV as a function of % movement cycle (Figure 6.3 A,B) and average CV over the entire experiment (Figure 6.3 C,D) were calculated for EFE and SAA to quantify progressive changes in movement variability. Comparison over the average movement cycle suggests that matched limb imitation yields lower CV in both the EFE and SAA. Additionally, over the length of the experiment, matched limb imitation shows lower average CV compared to mismatched limb imitation, particularly in the first half of movement trials. Halfway through the experiment, the difference in movement variability decreases and task performance becomes comparable between both groups.



**Figure 6.3:** Average CV for matched and mismatched imitation groups over movement cycle in EFE (A), SAA (B), and across all movement trials for EFE (C), SAA (D). Thin lines represent  $\pm$  one standard deviation about the mean (solid lines).

## Movement Duration

Average movement durations over the length of the experiment for each of the 20 groups of movements were calculated (Figure 6.4). Both groups show an initially longer movement duration that decreases over the length of the experiment. The matched limb imitation group, however, shows shorter movement durations, particularly in the first three quarters of the experiment. In the last quarter, the movement duration differences decrease and task performance becomes comparable.



**Figure 6.4:** Average movement duration across all movement trials for matched and mismatched imitation groups. Thin lines represent  $\pm$  one standard deviation about the mean (solid lines).

## Discussion

The goal of this chapter was to expand the findings of our previous kinematics work from Chapter 5 into a population of persons with amputation. The aim was to identify the behavioral effects of matched limb versus mismatched limb observation and imitation in these subjects and to provide further evidence for the relevance of action encoding concepts in this clinical population. Both during the average movement cycle and over the course of the experiment, matched limb imitation resulted in a lower movement variability in EFE and SAA, compared to mismatched limb imitation. Additionally, the matched limb imitation group performed movements with lower duration than their mismatched limb counterparts. Similar to the results of the same

experiment conducted previously in intact users of the FAMS, the current results suggest a behavioral advantage to matched imitation in persons with amputation using their prosthesis to perform a motor task. These findings have important implications on how prosthetic device operation is conveyed to persons with amputation during their initial rehabilitation and prosthesis training, as matched limb imitation yielded more consistent and prototypical movements with shorter duration.

There were several limitations in the current pilot study presented in this chapter. The particular task configuration chosen in this study (identical to that in Chapter 5) proved especially difficult for several of the subjects. In these subjects, the data suggest that the motor task itself was too difficult to elicit the documented pattern of initially high movement duration, followed by a decrease as a function of practice (Flament et al. 1999; Smeets 2000). In the subjects who were able to successfully complete the task, the variability metrics previously shown to be accurate measures of motor adaptation suggested beneficial effects of matched limb imitation. Future studies may involve less difficult motor tasks for persons with amputation to perform that more closely model ADLs and further illustrate the potential behavioral effects suggested here. It should also be noted that the data presented here represent persons with amputation who have a range of experience levels and daily prosthesis usage rates; both of which may impact the results.

An issue related to the difficulty of the motor task is the observation of moderate compensatory movements in subjects during the experiment. For example, active arm elevation was required in most subjects in order to accomplish the motor task with their prosthesis. This movement is described clinically as a “shoulder hike” and involves the



use of the trapezius muscle to lift the arm up and away from the torso by shrugging the shoulder blade. Another example of compensatory movement is the observation of lateral bending and torsional twisting of the spine. Due to the limited number of available channels for recording ELGON, these potentially important movements were not captured by the current data collection system. Work is underway to expand the number of recording channels available. Additionally, with the development of more feasible motor tasks for persons with amputation to perform, these compensatory movements can be minimized.

### **Conclusion**

The results of the current chapter suggest that there are beneficial effects of matched limb observation and imitation on the performance of motor tasks in persons with upper extremity amputations who use prosthetic devices. These pilot findings are important; as they suggest that the beneficial effects of matched limb imitation found in FAMS users may also be present in the clinical population of prosthesis users. This chapter contributes unique insights into the process of adapting to the functional constraints of a novel prosthetic limb and will be extended into a longitudinal FAMS training paradigm in the next chapter.

# **CHAPTER 7**

## **LONGITUDINAL NEURAL CORRELATES AND MOTOR BEHAVIOR OF ACTION OBSERVATION TRAINING IN PROSTHESIS USERS**

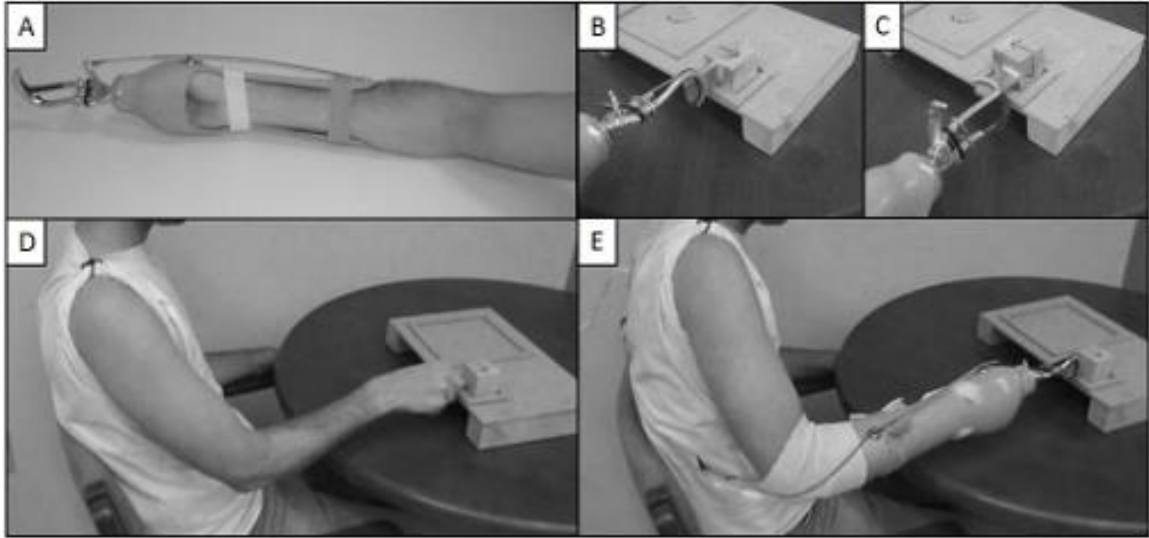
### **Introduction**

The work in Chapter 4 suggested that prosthesis users who imitated the movements of intact actors (mismatched limb imitation) elicit a unique set of cortical activations (Cusack et al. 2012). Instead of solely engaging the parietofrontal mechanism typically involved in planning and executing tool-use movements and pantomimes (Goldenberg et al. 2007; Hermsdorfer et al. 2007), activity was also observed in the right parietal and occipital cortical regions. It has been suggested that these parietooccipital areas are part of a mentalizing system that may be responsible for the visuomotor processing of unfamiliar and motor dissonant actions outside of one's own movement repertoire (Buccino et al. 2004a). Importantly, the typical pattern of parietofrontal system activity could be observed in prosthesis users, but only when they imitated actions performed by other prosthesis users with a matching prosthetic limb (matched limb imitation) (Cusack et al. 2012). Chapter 5 then implemented ELGON to investigate the behavioral effects of matched limb action imitation in intact users of the FAMS (Figure 7.1A). Users of the FAMS who performed matched limb imitation showed a decrease in shoulder motion variability compared to those who performed mismatched limb imitation.

The aim of this chapter is to combine the lessons from Chapters 4 and 5 to investigate the longitudinal effects of a matched limb imitation training paradigm on the cortical action encoding activity and motor behavior in intact users of the FAMS. The primary hypothesis is that matched limb training would result in greater longitudinal activity in the parietofrontal regions than mismatched limb training, which would show greater activity in the occipitoparietal regions. Secondly, due to the established importance of the parietofrontal system in planning and executing movements, the hypothesis states that matched limb training would result in reduced movement variability compared to mismatched limb training.

An important aspect of this training effort is action-observation therapy; a recently developed rehabilitation protocol that aims to enhance motor deficit rehabilitation through the observation of daily actions combined with concomitant physical training of the same observed actions (Ertelt et al. 2007). In action-observation therapy, patients carefully observe demonstrations of actions and then imitate the actions themselves. This form of training has been shown to have positive rehabilitative effects on motor performance in stroke survivors (Weiss et al. 1994; Page et al. 2001; Stevens and Stoykov 2003; Johnson-Frey 2004b; Ietswaart et al. 2006; Ertelt et al. 2007; Franceschini et al. 2010; Kim and Lee 2013), adults with Parkinson's disease (Pelosin et al. 2013), aphasia (Marangolo et al. 2012), and children with cerebral palsy (Sgandurra et al. 2013). The proposed mechanism underlying these beneficial results is a shared action encoding network in the motor-related cortical regions that is activated by both the observation and execution of a motor task (Ertelt et al. 2007). This training strategy provides an opportunity to further stimulate the cortical regions responsible for action

encoding through task-specific action observation. To our knowledge, action-observation training has not been applied to untrained users of prosthetic devices.



**Figure 7.1:** FAMS with Hosmer Model 5X Hook terminal device (A), workspace board and block used for motor task in starting position (B) and rotated 90° clockwise (C), screenshots of intact (D) and FAMS (E) video demonstrations observed by subjects.

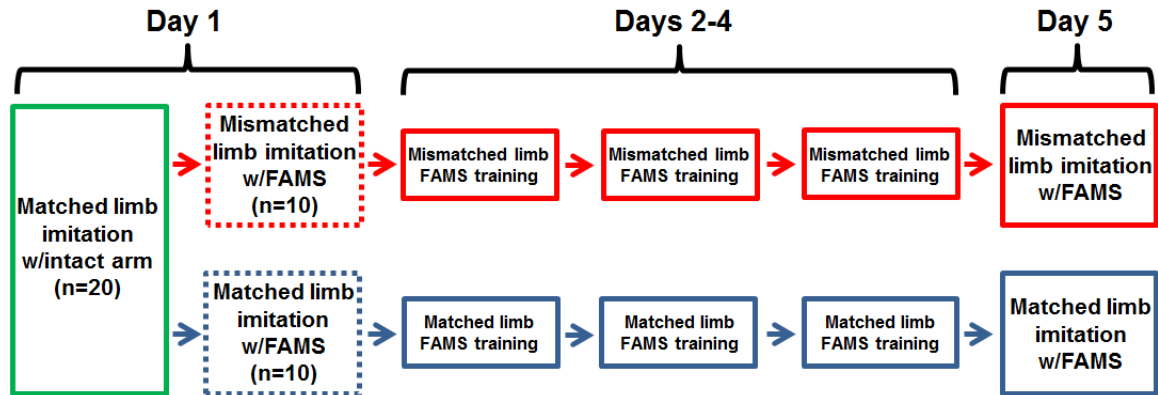
## Methods and Materials

### Subjects

Twenty right-handed intact subjects were recruited for this study (14 male, mean age =  $24.1 \pm 4.2$  years, range: 18-33 years). The Edinburgh Handedness Inventory (Oldfield 1971) was used to confirm handedness. Signed informed consent was acquired from all subjects according to the procedures set forth by the Institutional Review Board at The Georgia Institute of Technology.

## **Experimental Paradigm Overview**

The experimental paradigm required each subject to attend five sessions (Figure 7.2): an initial data collection (day 1), three rounds of prosthesis training (days 2-4), and a final data collection (day 5). Each session occurred on separate days, with the first and last session separated by a maximum of seven days. On day 1, all subjects first observed motor task demonstrations performed by an intact actor, and then imitated the demonstration with their right intact hand while EEG and joint angle kinematics were recorded (intact hand condition). Subjects were then immediately fitted with the FAMS device on the right arm (untrained FAMS condition) and randomly assigned to observe and imitate motor task demonstrations performed by either an intact actor (mismatched limb group) or a FAMS user (matched limb group). On each of days 2-4, subjects participated in action observation FAMS training, during which they observed and imitated matched or mismatched limb video demonstrations, according to their assigned group. On day 5, subjects wearing the FAMS on the right arm (trained FAMS condition) observed and imitated matched or mismatched limb motor task demonstrations according to their assigned group while EEG and ELGON were recorded. After each of the five sessions, subjects were asked to rate the perceived difficulty of performing the motor task with the FAMS on a scale of 1 (least difficult) to 10 (most difficult).



**Figure 7.2:** Diagram depicting experimental paradigm for matched (top row) and mismatched (bottom row) limb imitation training groups.

## FAMS

The FAMS is a specially adapted prosthesis socket that accommodates an intact subject's forearm and hand. The device is designed to simulate the altered degrees of freedom in the wrist and forearm that a transradial amputee would experience after the loss or reduction of those joints. The mode of operation is similar to what a transradial amputee using a prosthesis would experience. Namely, a cable system and shoulder harness allow for the terminal device to be opened by flexion and protraction of the shoulder, and closed by extension and retraction of the shoulder. Please see Chapter 5 for a complete description of the FAMS.

## Block Rotation Motor Task

Subjects viewed and imitated video demonstrations of a block rotation motor task adapted from the SHAP (Light et al. 2002). Please see Chapter 5 for a complete description of the task. With an intact arm, this task configuration typically involves

significant forearm pronation/supination and, to a lesser degree, wrist flexion/extension and wrist abduction/adduction. These degrees of freedom are eliminated or severely constrained by the FAMS. In order for FAMS users to imitate the observed task, they adapt modified joint control strategies in the elbow and shoulder; degrees of freedom that are unconstrained by the device. In Chapter 5, an identical task was successfully used to investigate motor performance in intact subjects adapting to use of the FAMS.

### **FAMS Training Sessions**

During the FAMS training sessions (days 2-4), subjects were seated in a chair of fixed height. A fixed-height workspace board (Figure 7.1B,C) was then positioned on a table in front of the subject such that the midline of the board was aligned with the vertical midline of the torso. The distance between the subject and the board was chosen such that the center of the workspace aligned with a fixed marker on the terminal device. Training sessions commenced with video presentation of either mismatched limb (Figure 7.1D) or matched limb (Figure 7.1E) demonstrations (according to their assigned group) which lasted 30 s and contained 15 movement repetitions. Subjects were instructed to remain motionless. Subjects fitted with the FAMS were then instructed to imitate the observed movements “as quickly and as accurately as possible” for two continuous minutes at a self-selected pace. This pairing of observation and imitation was repeated four times, with a break given at the half-way point to mitigate effects of fatigue. During each training session, each subject performed approximately 200 repetitions of the block rotation task.

Subjects completed a modified version of the MMDT (Lafayette Instrument, Lafayette, IN) throughout the course of training in order to evaluate motor performance

with the FAMS. Contrary to the block rotation task, this test required subjects to actively open and close the terminal device via the cabling system and shoulder harness. The test involved grasping and moving six numbered disks from the numbered spots on the left side of a workspace board to matching numbered spots on the right side of the board and then back again. Subjects were instructed to perform the task as quickly and as accurately as possible. Each test comprised of three rounds of the task and the duration of each was recorded with a stopwatch. The MMDT has been used previously to study improvements in motor impairment during rehabilitation and motor task training in hemiplegic stroke survivors (Lourencao et al. 2005; Bhatt et al. 2007; Lourencao et al. 2008; Pandian and Arya 2013) and adults with cerebral palsy (Hutzler et al. 2013).

### **Data Collection Sessions**

During the data collection sessions (days 1 and 5), subjects were fitted with a 58-channel EEG cap (Electrocap, Eaton, OH) that recorded scalp potential activity (1 kHz sampling rate, filtered at DC-100 Hz) via the Synamps 2 data acquisition system (Compumedics Neuroscan, Charlotte, NC). Electrooculography was recorded in two locations near the left eye to monitor eye blinks and movements. Three twin-axis electrogoniometers and one single-axis torsionmeter (models SG110/150 and Q110/Q150, respectively, Biometrics Ltd, Newport, UK) were fitted on the right arm of each subjects and connected to an 8-channel MyoSystem data collection system (model 1400L, Noraxon, Scottsdale, AZ, USA). ELGON data were sampled with 1 kHz frequency and 12 bit resolution.

There were six physiological degrees of freedom in the arm that were of interest in this study: wrist flexion/extension (WFE), wrist abduction/adduction (WAA), elbow



flexion/extension (EFE), shoulder abduction/adduction (SAA), horizontal shoulder flexion/extension (SFE), forearm supination/pronation (FRO), and shoulder internal/external rotation (SRO). Sensors were applied using guidelines provided by previous studies in upper extremity kinematics and the manufacturer's user manual (Chao et al. 1980; Anglin and Wyss 2000; Hansson et al. 2004; Wise et al. 2004; Magermans et al. 2005; Biometrics 2010). This methodology has been successfully employed for the study of upper limb joint motion during simulated activities ADLs (Chao et al. 1980; O'Neill et al. 1992). Further, the sensor configuration chosen for the current work was used successfully in our previous study that involved performance of the same block rotation task (see Chapter 5).

Subjects were seated comfortably and in the upright position in front of a workspace board as described above. A computer screen was placed 1.5 m away from the subject for the displaying video motor task demonstrations and written directions regarding movement cues. Both types of video lasted 30 s and contained 15 repetitions of the block rotation task. In an effort to allow naturalistic imitation movements, no explicit attempt was made to control the speed or pace of the subjects' movement repetitions. Initiation of the movements was controlled using a visual presentation cueing scheme developed in Stim (Compumedics Neuroscan, Charlotte, NC). Upon conclusion of the video demonstration, subjects remained motionless and fixated on a white cross for a randomly determined baseline period of 4.0-6.0 s. Subjects were then prompted to begin planning for the imitation movement upon seeing a "Get Ready!" cue that appeared for 1.0 s. A final cue then appeared cueing subjects to "Move!" and remained on the screen

for 10.0 s. This cued movement sequence was repeated 40 times, for a total of 200 individual repetition movements over a period of 11 minutes during each data collection.

### **Data Analysis**

Using Scan4.5 (Compumedics Neuroscan, Charlotte, NC, USA), continuous EEG data were band-pass filtered from DC-30 Hz. Data were then segmented into 3000 ms epochs capturing the 1500 ms preceding and 1500 ms following the presentation of the “Move!” cue that serves as the zero point for all EEG plot timelines. Linear detrending of the entire sweep and baseline correction with a baseline interval of -1600 ms s to -1100 ms s was then performed. Custom MATLAB (version R2012a, The MathWorks Inc., Natick, MA, USA) software was employed for artifact averaging and regression analysis to remove ocular movement artifacts (Semlitsch et al. 1986). An automated inspection rejected any epoch containing data outside a threshold range of -100 to 100  $\mu$ V.

Individual subject data were then averaged and grouped into the six experimental categories described by limb condition (intact hand, untrained FAMS, trained FAMS) and training group (mismatched limb, matched limb). Data were averaged over three 400 ms time windows corresponding to the phases of movement planning (-400 – 0 ms), early execution (200 – 600 ms), and late execution (600 – 1000 ms). The choice of these particular time windows was informed by our previous work (Chapter 4) in which cortical differences in prosthesis users were observed during a similar observation and imitation paradigm (Cusack et al. 2012). Data were further grouped into regions of interest that were defined in the left and right premotor areas (LPM: F3, F1, C5A, C3A, C1A; RPM: F4, F2, C6A, C4A, C2A), left and right motor areas (LM: C5, C3, C1; RM: C6, C4, C2), left and right parietal areas (LP: TCP1, P5, P3, P1, P3P; RP: TCP2, P6, P4,

P2, P4P), and occipital area (OCC: O1, OZ, O2) (Wheaton et al. 2005b; Cusack et al. 2012).

Using custom MATLAB software, all ELGON data were lowpass filtered at 6 Hz with a fourth-order Butterworth filter and then manually inspected on a subject level to identify the start and end of the individual movements. Each instance of peak shoulder abduction marked the start of the movement cycle and the following instance marked the end of that movement cycle. These instances correspond to behavioral transitions between counterclockwise and clockwise rotations in the block rotation task. Movements were averaged together into a representative movement for each of the 40 trials per data collection. All reported displacements are calculated relative to the reference displacement at the beginning of each movement.

The duration of each movement cycle was calculated, and then all angular displacement data were time normalized to percentage of the movement cycle. Duration data for the FAMS conditions are reported here as a percent change relative to the average movement duration of the intact hand condition. Positive percentage change indicates an increase in movement duration. Decreased movement duration over consecutive movement sessions has been shown to be an accurate measure for quantifying motor adaptation (Flament et al. 1999; Kempf et al. 2001; Smith et al. 2006). The CV for all 40 movement groups was calculated on a subject level according to  $CV(\%) = \sigma(\%)/\mu(\%)$ ; where  $\sigma(\%)$  and  $\mu(\%)$  are the angular displacement standard deviation and mean as functions of percent movement cycle, respectively. All reported CV values are calculated relative to the reference CV at the beginning of each movement.

Prior work has demonstrated that movements with lower variability are associated with better technique (Payton et al. 2007; Winter 2009).

### **Statistical Design**

For analysis of EEG data, a three-way mixed-model repeated measures ANOVA was separately applied to each of the three selected movement phases windows (planning, early execution and late execution). The between-subjects factors were electrode region of interest (LPM, RPM, LM, RM, LP, RP, OCC) and video (mismatched limb, matched limb). The within-subjects factors were electrode region of interest (LPM, RPM, LM, RM, LP, RP, OCC) and session (intact hand, untrained FAMS, trained FAMS).

Time series data ELGON were divided and averaged into eight contiguous time windows, each representing 12.5% of the complete movement cycle. Due to the symmetric nature of the task, this selection of time windows allowed for each to capture distinct phases of the movement profile. A three-way mixed model repeated measures ANOVA was performed with video and time window (1-8) as the between-subjects factors, and session as the within-subjects factor.

Movement duration, MMDT, and perceived difficulty data were compared using two-way mixed-model repeated measures ANOVAs with video as the between-subjects factor and session as the within-subjects factor. For all data types, subsequent post-hoc t-tests were performed with significance set at  $p < 0.05$  using Bonferroni correction. All statistical tests were conducted using SPSS Statistics software (version 19, The IBM Corporation, Armonk, NY, USA). The following codes will be referred to when describing the respective groups and conditions: Intact hand matched group = INT-MAT-

D1, intact hand mismatched group = INT-MIS-D1, untrained FAMS matched group = FAMS-MAT-D1, untrained FAMS mismatched group = FAMS-MIS-D1, trained FAMS matched group = FAMS-MAT-D5, trained FAMS mismatched group = FAMS-MIS-D5.

## **Results**

### **EEG**

ERPs for the three phases of interest were calculated to quantify longitudinal changes in cortical activity over the course of FAMS training (Figure 7.3). An ANOVA on planning phase data revealed a main effect of session ( $F(2) = 64.0, p < 0.001$ ), video ( $F(1) = 12.1, p < 0.001$ ), and electrode ( $F(6) = 16.6, p < 0.001$ ). An interaction effect was seen for session X video ( $F(2) = 8.56, p < 0.001$ ). The results of an ANOVA on early execution phase data showed a main effect of session ( $F(2) = 8.19, p < 0.001$ ), video ( $F(1) = 84.9, p < 0.001$ ), and electrode ( $F(6) = 43.8, p < 0.001$ ). An interaction effect was found for session X video ( $F(2) = 31.0, p < 0.001$ ). ANOVA of late execution phase data indicated a main effect of session ( $F(2) = 65.8, p < 0.001$ ), video ( $F(1) = 15.7, p < 0.001$ ), and electrode ( $F(6) = 74.3, p < 0.001$ ). An interaction effect was observed for session X video ( $F(2) = 35.2, p < 0.001$ ).

### Effects of Video Imitation Type

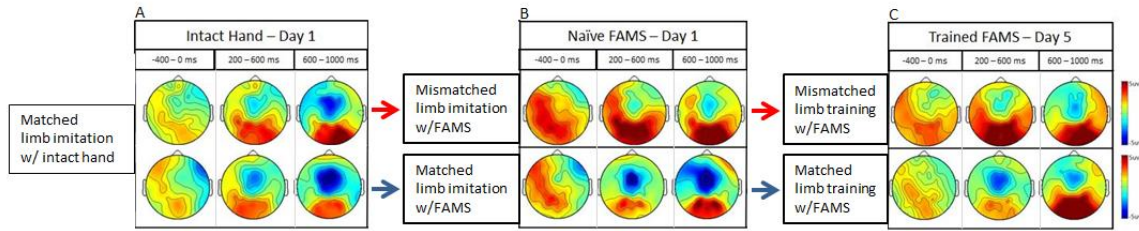
Between-subjects ANOVAs allowed for the comparison of cortical activity between training groups for each of the limb conditions (intact hand, untrained FAMS, trained FAMS).

Before donning the FAMS for the first time, all subjects observed video demonstrations of an intact hand and then imitated these movements with their own intact

hand. A comparison for this intact hand condition was made between those subjects who would later be separated into the matched and mismatched limb training groups (Figure 7.3A). Post-hoc analyses indicated no differences in activity in any of the cortical regions of interest for the planning, early execution, or late execution phases.

Subjects next donned the FAMS for the first time and performed either matched or mismatched limb imitation, based on their assigned group. A comparison between these two groups was made in order to investigate the effects of video type on cortical activity prior to training (untrained FAMS) (Figure 7.3B). Post-hoc analyses indicated greater negativity for the matched limb imitation group in: RPM, RP, and OCC for the planning phase (all comparisons  $F(1) \geq 4.12$ ,  $p \leq 0.043$ ); LPM, RPM, LM, RM, LP, RP, and OCC for the early execution phase (all comparisons  $F(1) \geq 12.4$ ,  $p < 0.001$ ); LPM, RPM, LM, RM, and RP for the late execution phase (all comparisons  $F(1) \geq 5.24$ ,  $p \leq 0.022$ ).

On day 5 (once training was complete), subjects donned the FAMS and again performed matched or mismatched limb imitation, based on their assigned group. A comparison between these two groups was made in order to investigate the effects of video type on cortical activity in the FAMS condition once training was completed (Figure 7.3C). Post-hoc analyses revealed greater negativity for the matched limb imitation group in: RP for the planning phase ( $F(1) = 8.30$ ,  $p = 0.0040$ ); LPM, RPM, LM, RM, LP, RP, and OCC for the early execution phase (all comparisons  $F(1) \geq 4.63$ ,  $p \leq 0.032$ ); LP for the late execution phase ( $F(1) = 6.60$ ,  $p = 0.010$ ).



**Figure 7.3:** Grand-averaged electrode headplots for all experimental conditions. For each condition, data were averaged over three 400 ms time windows corresponding to the phases of movement planning (-400 – 0 ms), early execution (200 – 600 ms), and late execution (600 – 1000 ms).

### Longitudinal Effects of Video Training Type

Within-subjects ANOVAs allowed for the comparison of cortical activity within each respective group as the training progressed. There are two within-subjects comparisons of interest: intact hand versus untrained FAMS (referred to as effect of FAMS) and untrained FAMS versus trained FAMS (referred to as effect of training). Throughout the progression of the experiment, there were several effects on cortical activity that occurred in both mismatched limb (Figure 7.4A) and matched limb training groups (Figure 7.4B); all of which were exclusive to the left hemisphere. In addition to the effects on cortical activity common to both groups, there were several effects that were unique to each group (Figure 7.5 and Figure 7.6).

### Effect of FAMS

Post-hoc analyses showed an effect of FAMS in both groups that involved reduced negativity in: LPM, LM, and LP for the planning phase (all comparisons  $F(2) \geq 4.10$ ,  $p \leq 0.018$ ); LP for the late execution phase (all comparisons  $F(2) \geq 4.71$ ,  $p \leq 0.010$ ). Exclusive to the mismatched limb group, post-hoc analyses indicated an effect of FAMS

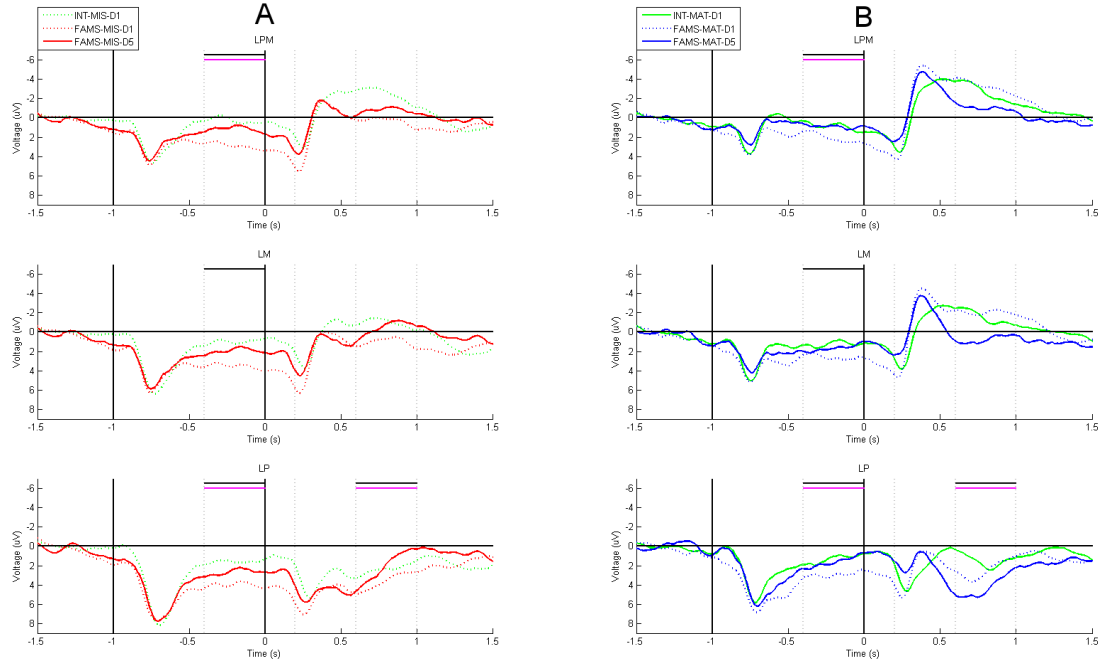
that involved decreased negativity in: RPM, RM, RP, OCC for the planning phase (all comparisons  $F(2) \geq 4.71$ ,  $p \leq 0.010$ ); LPM, RPM, LM, LP, RP, OCC for the early execution phase (all comparisons  $F(2) \geq 3.25$ ,  $p \leq 0.041$ ); LPM, RPM, LM, RM, RP, OCC for the late execution phase (all comparisons  $F(2) \geq 3.50$ ,  $p \leq 0.032$ ) (Figure 7.5).

### Effect of Training

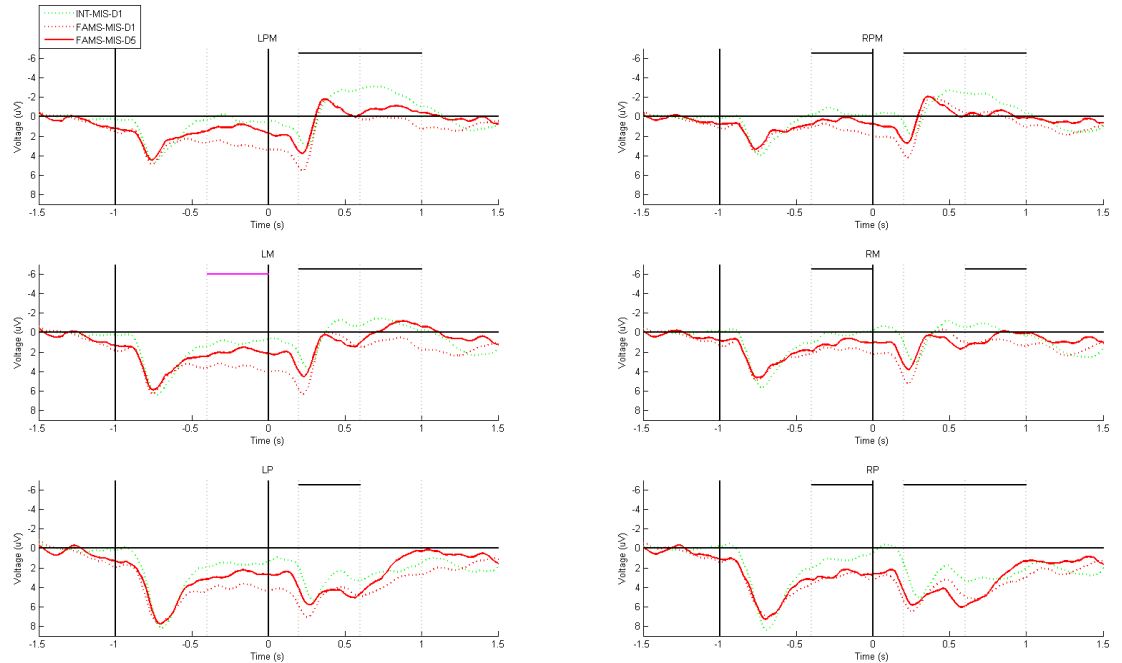
Post-hoc analyses indicated an effect of training in both groups that included increased negativity in: LPM and LP for the planning phase (all comparisons  $F(2) \geq 3.94$ ,  $p \leq 0.021$ ); LP for the late execution phase (all comparisons  $F(2) \geq 3.41$ ,  $p \leq 0.042$ ). Exclusive to the mismatched limb group, post-hoc analyses revealed an increase in negativity due to training in the: LM for the planning phase (all comparisons  $F(2) = 9.46$ ,  $p = 0.012$ ) (Figure 7.5). Exclusive to the matched limb group, post-hoc analyses demonstrated an effect of training that included decreased negativity in: LPM, RPM, LM, RM, RP, OCC for the late execution phase (all comparisons  $F(2) \geq 5.98$ ,  $p \leq 0.003$ ) (Figure 7.6).

To summarize, in the mismatched group, donning of the FAMS affected the only the right hemisphere in the planning phase, and affected both hemispheres in the execution phases. There were minimal effects of training in either hemisphere during movement planning or execution. In the matched group, training with the FAMS affected both hemispheres in the late execution phase. There were no effects of donning the FAMS in either hemisphere during movement planning or execution.

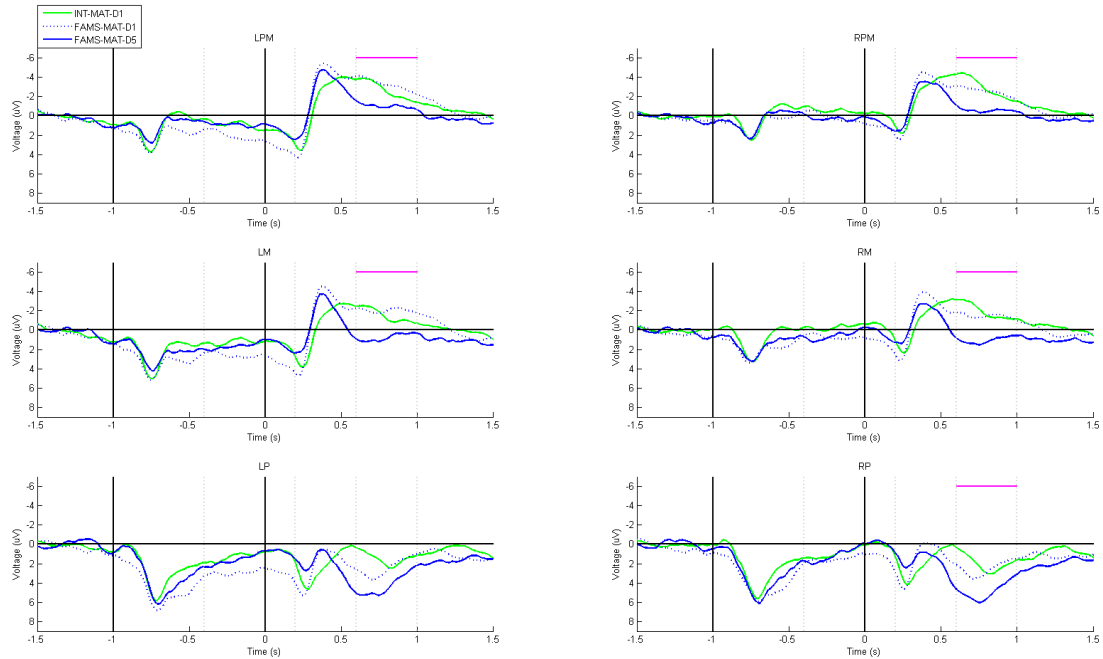




**Figure 7.4:** Grand-averaged region-level voltage plots showing the common longitudinal effects observed (exclusive to the left hemisphere) for both mismatched (A) and matched (B) limb imitation training groups. The presentation of the “Get Ready” and “Move” cues are marked with vertical black lines at -1.0 and 0.0 s, respectively. Time windows corresponding to the phases of movement planning (-400 – 0 ms), early execution (200 – 600 ms), and late execution (600 – 1000 ms) are marked with gray vertical lines. There are two comparisons of interest: intact hand versus untrained FAMS (significant differences marked with horizontal black lines,  $p < 0.05$ ) and untrained FAMS versus trained FAMS (significant differences marked with horizontal pink lines,  $p < 0.05$ ).



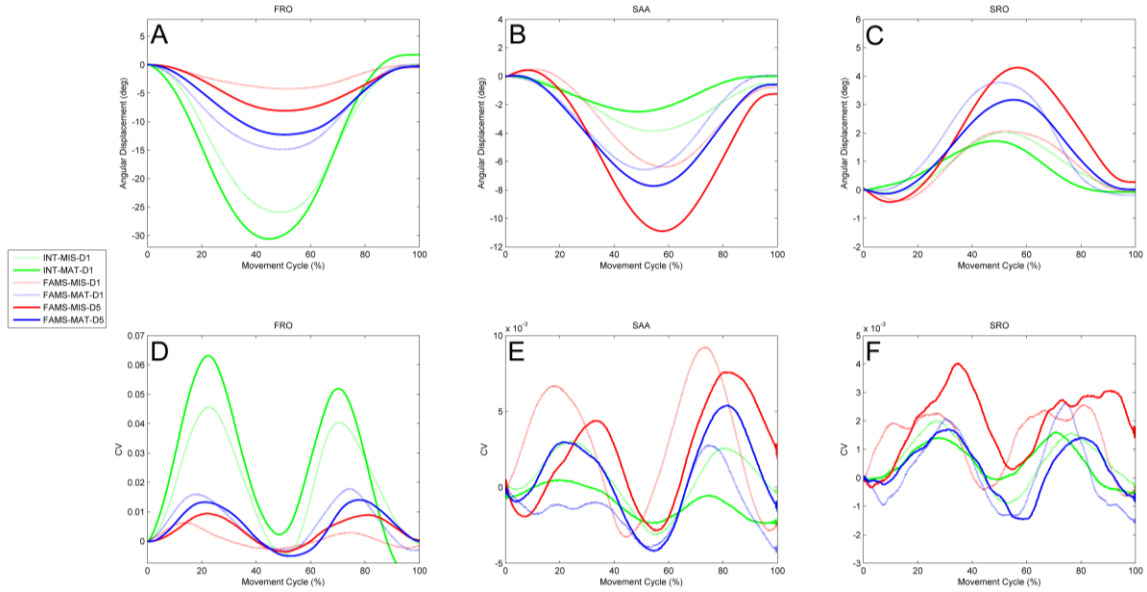
**Figure 7.5:** Grand-averaged region-level voltage plots showing the longitudinal effects observed exclusively in the mismatched limb imitation training groups. The presentation of the “Get Ready” and “Move” cues are marked with vertical black lines at -1.0 and 0.0 s, respectively. Time windows corresponding to the phases of movement planning (-400 – 0 ms), early execution (200 – 600 ms), and late execution (600 – 1000 ms) are marked with gray vertical lines. There are two comparisons of interest: intact hand versus untrained FAMS (significant differences marked with horizontal black lines,  $p < 0.05$ ) and untrained FAMS versus trained FAMS (significant differences marked with horizontal pink lines,  $p < 0.05$ ).



**Figure 7.6:** Grand-averaged region-level voltage plots showing the longitudinal effects observed exclusively in the matched limb imitation training groups. The presentation of the “Get Ready” and “Move” cues are marked with vertical black lines at -1.0 and 0.0 s, respectively. Time windows corresponding to the phases of movement planning (-400 – 0 ms), early execution (200 – 600 ms), and late execution (600 – 1000 ms) are marked with gray vertical lines. There are two comparisons of interest: intact hand versus untrained FAMS (significant differences marked with horizontal black lines,  $p < 0.05$ ) and untrained FAMS versus trained FAMS (significant differences marked with horizontal pink lines,  $p < 0.05$ ).

## **Movement Angular Displacement**

The FAMS eliminates or significantly limits several degrees of freedom in the limb. FAMS users adapt alternative control strategies in the remaining degrees of freedom to imitate the observed task successfully. Figure 7.7A-C shows the group-level angular displacements at several degrees of freedom during performance of the block rotation task in all three conditions: intact hand, untrained FAMS, and trained FAMS. Displacement data ANOVAs revealed main effects of session on the movement profiles of WFE ( $F(2) = 7.85, p < 0.001$ ), WAA ( $F(2) = 12.5, p < 0.001$ ), SAA ( $F(2) = 53.6, p < 0.001$ ), SFE ( $F(2) = 6.78, p < 0.0020$ ), FRO ( $F(2) = 101, p < 0.001$ ), and SRO ( $F(2) = 11.8, p < 0.001$ ). No main effect of session was found on EFE ( $F(2) = 1.08, p = 0.34$ ). Behaviorally, the intact hand data features extensive range of motion in wrist flexion/extension, wrist adduction/abduction, and forearm supination/pronation (Figure 7.7A); all of which are significantly reduced once donning the FAMS. In response, the task is performed with the FAMS with significantly increased range of motion in shoulder abduction/adduction (Figure 7.7B), shoulder flexion/extension, and shoulder rotation (Figure 7.7C).



**Figure 7.7:** Angular displacements and CV for FRO (A,D), SAA (B,E) and SRO (C,F), respectively.

## Movement CV

Relative CV as a function of percent movement cycle was calculated for each degree of freedom to quantify progressive changes in movement variability over the course the experiment (Figure 7.7D-F).

## Elbow Flexion/Extension (EFE)

An ANOVA of EFE CV data revealed a main effect of session ( $F(2) = 5.91$ ,  $p = 0.0030$ ) and no main effect of video ( $F(1) \leq 0.0240$ ,  $p = 0.88$ ) or interaction effect of session X video ( $F(2) = 1.45$ ,  $p = 0.24$ ). Behaviorally, this result corresponds to a significant increase in CV from the intact hand condition ( $0.5e-3$ ) to the FAMS conditions (untrained:  $2.4e-3$ , trained:  $2.1e-3$ ).

### Shoulder Abduction/Adduction (SAA)

The results of an ANOVA on SAA CV data (Figure 7.7E) indicated main effects of session ( $F(2) = 5.23, p = 0.0060$ ) and video ( $F(1) = 14.8, p < 0.001$ ), but no interaction effect of session X video ( $F(2) \leq 1.37, p = 0.26$ ). Behaviorally, this result again corresponds to a significant increase in CV from the intact hand condition ( $-0.2e-3$ ) to the FAMS conditions (untrained:  $0.7e-3$ , trained:  $1.4e-3$ ). Additionally, this degree of freedom showed less movement CV in the matched ( $-0.5e-3$ ) versus mismatched imitation ( $1.8e-3$ ) group.

### Shoulder Flexion/Extension (SFE)

ANOVA on SFE CV data showed no main effect of session ( $F(2) = 1.99, p \geq 0.14$ ), but did show a main effect of video ( $F(1) = 9.99, p = 0.0020$ ) and interaction effect of session X video ( $F(2) = 5.47, p = 0.0050$ ). Post-hoc analyses again showed less movement CV in matched ( $-0.57e-3$ ) versus mismatched imitation ( $0.1e-3$ ) during the untrained FAMS condition ( $F(2) = 11.6, p < 0.001$ ).

### Shoulder Internal/External Rotation (SRO)

An ANOVA of SRO CV data (Figure 7.7F) demonstrated no main effect of session ( $F(2) = 1.16, p = 0.32$ ) but did reveal a main effect of video ( $F(1) = 7.84, p = 0.0060$ ), with no interaction effect of session X video ( $F(2) = 2.79, p = 0.064$ ). Behaviorally, this result again corresponds to less movement CV in the matched ( $0.3e-4$ ) versus mismatched imitation ( $1.3e-3$ ) group.

### Forearm Pronation/Supination (FRO)

The results of an ANOVA on FRO CV data (Figure 7.7D) revealed main effects of session ( $F(2) = 67.0, p < 0.001$ ) and video ( $F(1) = 13.7, p < 0.001$ ), as well as interaction effect of session X video ( $F(2) = 3.52, p = 0.032$ ). Behaviorally, this result corresponds to a significant decrease in CV from the intact hand condition ( $2.2e-2$ ) to the FAMS conditions (untrained:  $3.0e-3$ , trained:  $4.0e-3$ ). Additionally, post-hoc analyses showed greater movement CV in matched ( $6.0e-3$ ) versus mismatched imitation ( $1.0e-3$ ) during the untrained FAMS condition ( $F(2) = 43.5, p < 0.001$ ).

### **Movement Duration**

Relative to performance with the intact hand, subjects showed overall increases in movement duration during the untrained FAMS ( $13.7 \pm 2.6\%$ ) and trained FAMS condition ( $11.4 \pm 3.1\%$ ). Despite the trend of decreasing movement duration with additional FAMS training, ANOVA revealed no main effect of session ( $F(1) = 0.316, p = 0.58$ ). Matched limb imitation showed an overall increase in movement duration ( $14.4 \pm 2.6\%$ ) compared to that of mismatched limb imitation ( $10.6 \pm 3.2\%$ ), but no main effect of video was found ( $F(1) \leq .855, p = 0.36$ ). No interaction effect of session X video was observed ( $F(1) = 0.020, p = 0.89$ ).

### **MMDT**

An ANOVA of MMDT performance data revealed a main effect of session ( $F(3) = 118, p < 0.001$ ), but no main effect of video ( $F(1) = 2.46, p = 0.12$ ) or interaction effect of session X video ( $F(3) = 0.848, p = 0.47$ ). Overall, subjects' MMDT time decreased significantly after each FAMS training session (pre-day 2 =  $48.2 \pm 1.3s$ ; post-day 2 =  $40.5 \pm 1.1s$ ; post-day 3 =  $35.2 \pm 0.8s$ ; post-day 4 =  $32.0 \pm 0.8s$ ).

### **Perceived Difficulty of Block Rotation Task**

The results of an ANOVA on perceived difficulty of block rotation task revealed a main effect of session ( $F(4) = 16.2, p < 0.001$ ), but no main effect of video ( $F(1) = 0.454, p = 0.51$ ) or interaction effect of session X video ( $F(4) = 0.479, p = 0.75$ ). Overall, subjects' perceived difficulty decreased significantly or remained nearly constant after each exposure to the FAMS (day 1 =  $6.6 \pm 0.5$ s; day 2 =  $5.3 \pm 0.4$ s; day 3 =  $4.0 \pm 0.4$ s; day 4 =  $4.0 \pm 0.5$ s; day 5 =  $3.3 \pm 0.4$ s).

### **Discussion**

The goal of this chapter was to determine the longitudinal effects of a matched limb imitation training paradigm on the cortical action encoding activity and motor behavior in intact users of the FAMS. FAMS training occurred over three sessions and contained trials of action observation followed by action imitation. Participants in the matched and mismatched limb groups exclusively watched video demonstrations by either a prosthesis user or an intact actor, respectively. EEG and ELGON were recorded longitudinally in order to track changes in cortical activity and movement variability. After the first imitation session, matched limb subjects showed increased engagement of the parietofrontal system while mismatched limb subjects showed greater engagement of the parietooccipital system compared to the use of the intact hands. Longitudinally, the matched limb imitation group showed a reduction in bilateral parietofrontal negativity to levels similar to the intact hands. The mismatched limb imitation group exhibited minimal effects of FAMS training on cortical activity longitudinally, and exhibited continued bilateral parietooccipital activation. Over the course of the paradigm, matched limb imitation subjects also showed lower movement variability compared to those



trained with mismatched limb imitation. Together, these results indicate that matched limb imitation may play an important neurobehavioral role in both the processes of prosthetic device training and rehabilitation.

### **Effects of FAMS on Motor Task Kinematics**

Comparison of each subject's joint kinematics between the intact hand and untrained FAMS conditions revealed the effect of wearing the prosthesis on motor task performance. The results showed that the range of motion was significantly reduced and/or constrained by the FAMS in wrist flexion/extension, wrist adduction/abduction, and forearm supination/pronation. These kinematic restrictions were compensated for by changes to the range of motion in the remaining unconstrained degrees of freedom: shoulder abduction/adduction, shoulder flexion/extension, and shoulder rotation. As argued in Chapter 5, this loss of distal degrees of freedom and compensation by proximal degrees of freedom is a reasonable model for the kinematic changes occurring after upper extremity amputation and subsequent prosthesis use. Beyond changes in angular displacement, use of the FAMS also resulted in changes in movement variability in several degrees of freedom. Overall decrease in variability in forearm supination/pronation is expected due to the severe movement limitations imposed by the FAMS. Similar to Chapter 5, elbow flexion/extension and shoulder adduction/abduction also exhibited increased movement variability during use of the FAMS. Finally, relative to performance with the intact hand, subjects showed overall increases in movement duration during the untrained FAMS condition, which may reflect the additional difficulty of performing the familiar motor task with a novel set of kinematic constraints.

## **Effects of Video Imitation Type**

In agreement with the hypothesis, during the early execution and late execution phases in the untrained FAMS condition, matched limb subjects showed greater engagement of the bilateral parietofrontal system while mismatched limb subjects showed greater engagement of the bilateral parietooccipital system. Once FAMS training was complete, these group differences remained consistent and occurred primarily in the early execution phase. This finding aligns with our prior studies, suggesting that activation of the typical parietofrontal action encoding system is possible in prosthesis users, but only when they are able to imitate a limb state that matches their own (Cusack et al. 2012). Further, without such a match, the planning phase can no longer occur as normal and relies more heavily on the parietooccipital action encoding system.

Prior studies have shown that specific areas within the premotor, motor, and parietal cortices are active when planning, executing and observing cognitive motor control tasks (Cattaneo and Rizzolatti 2009). This network of parietofrontal cortical regions may provide a mechanism by which we can understand, learn, and imitate the actions of others from within using our own perspective (Rizzolatti and Sinigaglia 2010). In this neural framework, it is hypothesized that observation of an action drives an internal replication of that action in the motor system of the observer in a somatotopic manner. Further, it has been proposed that the degree to which the parietofrontal system is engaged is a function of the motor resonance between the observed and the observer (Buccino et al. 2001).

In Chapter 4, intact subjects showed equivalent left parietofrontal activity during imitation planning after watching the intact or prosthetic arm. Likewise, when prosthesis

users imitated prosthesis demonstrations, typical left parietofrontal activation was observed. When prosthesis users imitated intact actors, an additional pattern was revealed which showed greater activity in right parietal and occipital regions that are associated with the mentalizing system. This change may be required for prosthesis users to plan imitation movements in which the limb states between the observed and the observer do not match. The finding that prosthesis users imitating other prosthesis users showed typical left parietofrontal activation suggests that these subjects engage normal planning related activity when they are able to imitate a limb matching their own. The results suggest that the potential sensitivity of the parietofrontal action encoding areas to the differences in kinematic ability and appearance between the observer and the observed is a particularly relevant finding for users of prostheses who imitate the mismatched actions of an intact limb.

Differences in movement variability based on the type of limb imitated were also observed. Overall, matched limb imitation showed less movement CV in shoulder adduction/abduction, flexion/extension, and internal/external rotation compared to mismatched limb imitation. Prior work has demonstrated that movements with lower variability have been associated with better technique and more effective movement strategy formation (Payton et al. 2007; Winter 2009). In alignment with the hypothesis, this result suggests a behavioral advantage to matched imitation, as it yielded more consistent and prototypical movements in the joint principally responsible for adapting to the novel FAMS kinematics. As described previously in intact subjects, parietofrontal network activity is important for the planning and execution of tool-use movement and imitation (Goldenberg et al. 2007; Hermsdorfer et al. 2007; Cattaneo and Rizzolatti 2009;

Tsuda et al. 2009; Rizzolatti and Sinigaglia 2010). Enhanced motor resonance can also account for activation of the corticospinal pathways and task-specific muscles during action observation (Strafella and Paus 2000; Funase et al. 2007; Alaerts et al. 2009). It is suggested that in the case of the matched limb imitation group, observing the movements with greater motor resonance and functional congruity enhanced the engagement of the parietofrontal action encoding system and better facilitated the formation of the new movement strategy.

Contrastingly, additional parietooccipital activity in the mismatched limb group may reflect an increased visuospatial demand of the imitation motor task (Buccino et al. 2004a). The influence of FAMS training type on the relative activity in the parietofrontal versus occipitoparietal action encoding systems may explain the differences in movement variability observed in the current study. This result and interpretation is corroborated with our previous study, in which mismatched limb imitation resulted in a greater shoulder adduction/abduction variability compared to matched limb imitation (see Chapter 5).

### **Longitudinal Effects of Video Training Type**

Longitudinally, both training groups revealed several common effects throughout the experiment. Each group showed an increase in activity in the left parietofrontal areas as well as the left motor region during first-time FAMS use. This result corroborates a previous study in which direct exposure to a novel tool yielded increased activations of the bilateral parietofrontal areas (Mizelle et al. 2011). This suggests that subjects in both training groups activated the canonical parietofrontal regions involved with tool use (Johnson-Frey 2004a); which is expected due to the nature of the tool-use task in the

current paradigm. The next similarity between the two training groups is a decrease in activity in left parietofrontal areas after completion of the respective FAMS training paradigms. These results again agree with the existing literature that suggests the learning of new motor sequences is accompanied by an increase in activity in the presupplementary motor, premotor, parietal, and prefrontal areas, and is then followed by a decrease in activity in these same areas as the motor sequence becomes more automatic (Toni et al. 1998; Wu et al. 2004; Liew et al. 2013). Behaviorally, there was a trend of decreasing movement duration between the untrained and trained FAMS condition that may be an indication of enhanced performance. This result is corroborated by our previous work in Chapter 5 using this same motor task, in which we showed a trend of decreased movement duration after FAMS practice. Further evidence of enhanced FAMS performance over the course of the current experiment is provided by significantly improved MMDT times and decreased perceived difficulty of the motor task.

Beyond these common effects, mismatched limb imitation uniquely showed widespread increased right premotor, motor, parietal, and occipital activity during the planning phase during untrained FAMS use. As suggested in earlier chapters, this increased activity in right parietooccipital areas may be indicative of a greater degree of visual comprehension required to complete the goal-directed movement. In the context of the current study, it is suggested that the mismatched limb imitation group yielded less motor resonance with the novel FAMS task compared to the matched limb imitation group, which showed no such increase in right parietooccipital areas upon untrained FAMS use. Contrastingly, matched limb imitation group uniquely showed longitudinal decreases in bilateral premotor and motor activity after training was complete, while the

mismatched limb imitation group revealed no effects of training. As described above, a decrease in activity in these areas is expected as the motor task becomes learned and thus, it is suggested that matched limb imitation is more effective at facilitating automaticity of a novel motor task (Toni et al. 1998; Wu et al. 2004; Liew et al. 2013). The behavioral data discussed above support this interpretation, as matched limb imitation resulted in lower variability in several dimensions of shoulder movement.

### **Conclusion**

The results of this chapter demonstrate that the parietofrontal action-encoding network is preferentially engaged by matched limb action-observation training in novel users of a prosthetic device, and that this cortical activity is accompanied with beneficial effects in motor performance. Mismatched limb imitation may lead to decreased engagement of the typical parietofrontal action-encoding network and decreased motor task performance. These findings have a number of important clinical implications, as it has been proposed that deviations in normal neural control strategies may influence the degree to which a patient successfully incorporates their device into ADLs (Cohen et al. 1991; Rossini et al. 2011). Second, to our knowledge, this work provides the first evidence supporting the notion that action-observation therapy that provides the opportunity to observe and imitate actions performed by another prosthesis user may be beneficial to persons with limb amputation training to use upper extremity prostheses. The final chapter will elaborate on implications for the field of motor control and potential clinical applications in persons with upper extremity amputation.

## **CHAPTER 8**

### **CONCLUSIONS AND FUTURE WORK**

#### **Integration of Dissertation Findings**

There were over 1.5 million persons with amputation living in the US in 2005. Within that population, 548,000 individuals exhibited upper limb amputation. For a number of reasons including, but not limited to, the increased prevalence of diabetes-related amputations, the total number of persons with amputation is projected to rise to at least 2.2 million by 2020 (Dillingham et al. 2002; Ziegler-Graham et al. 2008; Barmparas et al. 2010; McFarland et al. 2010; Resnik et al. 2012). In order to maintain their quality of life, it is beneficial for persons with amputation to learn how to successfully perform ADLs with their artificial limb. Unfortunately, a recent meta-analysis revealed that full functional adoption of prostheses is low, with persons with upper extremity amputations rejecting their myoelectric, body-powered, and passive devices at mean rates of 23%, 26%, and 39% respectively (Biddiss and Chau 2007a; Biddiss and Chau 2007b). Thus, despite the attention and resources provided to development of more advanced myoelectric prosthetic devices with enhanced functionality, device rejection rates remain comparable to those of traditional body-powered prostheses.

The focus of this dissertation was instead placed on expanding the neuroscience foundation of rehabilitation in prosthesis users. While there is currently no consensus on the specifics of upper extremity prosthesis training in terms of intensity, frequency, or duration, a main tenet of most protocols is the practice of repetitive and active movements (Smurr et al. 2008; Resnik et al. 2012). In a recent protocol article by Smurr

et al., the authors stated that an integral component of body-powered and myoelectric prosthesis training protocols for persons with all levels of upper extremity amputation is to “mimic motion of therapist for shoulder, elbow, and terminal device control.” Thus, from the onset of their training, amputees are tasked with learning to use their device from an individual with two sound limbs. This, by default, results in a scenario similar to that described above where an amputee imitates motor tasks performed by an intact limb (Smurr et al. 2008). Based on current knowledge of action encoding mechanisms in the human motor system described in previous chapters, this basic aspect of the rehabilitation process may be problematic for new users of prosthetic devices and thus warrants investigation.

The central hypothesis of this dissertation was that in order to optimally engage the typical parietofrontal network during action imitation with a prosthetic device, the action being imitated should be performed by a matching prosthetic limb. Further, it was predicted that greater engagement of the typical parietofrontal network will result in increased ability to successfully plan and execute tool-use movements. The goal of this dissertation was to use basic neuroscience findings to inform the development of improved rehabilitation protocols that lead to greater functional adaptation of upper extremity prosthetic devices into the lives of persons with amputation. This dissertation has contributed unique findings to address the fundamental neuroscience questions outlined above.

First, in Chapter 4 we demonstrated that when prosthesis users imitated prosthesis demonstrations, typical left parietofrontal activation was observed. Contrastingly, when prosthesis users imitated intact actors, an additional pattern was revealed which showed



greater activity in right parietal and occipital regions that are associated with the mentalizing system. This change may be required for prosthesis users to plan imitation movements in which the limb states between the observed and the observer do not match. The finding that prosthesis users imitating other prosthesis users showed typical left parietofrontal activation suggests that these subjects engage normal planning related activity when they are able to imitate a limb that matches their own. We proposed that this unique activation pattern could have behavioral consequences during development of motor patterns in prosthesis users during therapist-led training with intact hands.

Second, in Chapter 5 we aimed to identify the behavioral effects of matched versus mismatched limb action imitation in intact users of the FAMS. Matched imitation resulted in a significant decrease in shoulder motion variability compared to mismatched imitation. Further, the matched group developed elbow motion patterns similar to the FAMS demonstrator, while the mismatched group attempted patterns similar to the intact demonstrator. This suggests a behavioral advantage to matched imitation when adapting to a prosthetic device, as it yielded more consistent movements and facilitated development of new motor patterns.

In Chapter 6 we expanded the matched versus mismatched limb imitation paradigm from Chapter 5 into a population of persons with amputation. This would provide further evidence for the relevance of action encoding concepts in this clinical population. Both during the average movement cycle and over the course of the experiment, matched limb imitation resulted in a lower movement variability in elbow and shoulder motion, compared to mismatched limb imitation. Additionally, the matched

limb imitation group performed movements with lower duration than their mismatched limb counterparts.

Finally, in Chapter 7 we investigated changes in cortical activity and corresponding motor behavior longitudinally in FAMS users trained with either matched limb or mismatched limb imitation over the course of five days. Matched limb trained subjects showed greater engagement of the parietofrontal system while mismatched limb trained subjects showed greater engagement of the parietooccipital system. Further, the matched limb imitation group showed a longitudinal reduction in bilateral parietofrontal negativity while the mismatched limb imitation group exhibited minimal effects of FAMS training on cortical activity. Over the course of the paradigm, matched limb trained subjects also showed lower movement variability compared to those trained with mismatched limb imitation.

Taken together, these results support the central hypothesis that matched limb observation may play an important role in the process of planning and executing motor tasks using a prosthetic device. Effects include increased engagement of the typical parietofrontal action encoding system and reduced movement variability during the task performance. These results disprove the alternative hypothesis that stated observation and imitation of both a matched and a mismatched prosthetic limb equivalently engages the parietofrontal network during action imitation with a prosthetic device. Further, the alternative hypothesis that prosthesis users demonstrate equivalent ability to perform action imitation movement despite differentially engaging the parietofrontal versus parietooccipital action encoding networks was also disproven.

An important finding in this dissertation is that the relative engagement of the parietofrontal and parietooccipital action encoding networks can be influenced by matched limb imitation in both persons with amputation using their prostheses and in intact subjects using the FAMS. This outcome supports a larger concept of how prosthetic devices may be incorporated into the cortical representations of the body.

## **Implications for Motor Control**

### **Engaging the Parietofrontal Network**

These interpretations are perhaps best discussed in the context that the parietofrontal action encoding network receives inputs from two distinct sets of cortical regions in the anterior and posterior brain, each with their own crucial functions. Information regarding attention, motivation, and goal selection is received from the prefrontal areas and the selection of appropriate action goals is mediated by the pre-supplementary motor and premotor areas (Buch et al. 2012). Contrastingly, information regarding the current limb state and progress towards achieving the action goal is integrated and transmitted from the inferior and superior posterior parietal cortex (Buch et al. 2012).

Activity in the parietal motor-related systems is associated with sensorimotor transformations during limb movement and will be involved to a certain degree regardless of the type of limb being imitated (Menz et al. 2009). However, as this dissertation has shown, activity in the frontal motor-related areas is partially dictated by the level of motor resonance in the action being imitated. In the absence of such motor resonance, there appears to be an increased dependence on the visuomotor network. The work presented here suggests that while both types of video demonstration result in

successful imitations, the groups that engaged the parietofrontal network did so with more stereotypical movement and lower variability.

These findings are significant to the field of motor control as they suggest that in order to more optimally engage the parietofrontal network, facilitation of inputs from frontal motor-related cortical systems is beneficial. Furthermore, current rehabilitation methods which include mismatched limb imitation and repetitive practice may not optimally engage the parietofrontal network from the frontal motor-related areas. The clinical significance of this notion is that enhancing the engagement of frontal motor-related systems can lead to more effective movement planning.

The respective engagement of the left parietofrontal and right parietooccipital networks has been previously studied in a variety of contexts. In a study by Buccino et al. (2004), subjects observed several mouth actions performed by monkeys, dogs, and other humans (Buccino et al. 2004a). Results showed activation of the parietofrontal network upon observation of actions that belonged to the subject's own motor repertoire (biting, for example), while actions outside of the motor repertoire (barking, for example) elicited activation of the parietooccipital network. The authors concluded that the activity of the parietofrontal network is somewhat dependent on the match between the motor repertoire of the observer and the observed. The results presented in this dissertation add to this concept by demonstrating that changes to a subject's limb state via use of a prosthesis can alter what is considered a matched motor repertoire from an internal perspective. Together, the results show that a matched motor repertoire may be achieved by modifications to the limb state of the observer and/or the observed.

### **Updating Cortical Limb Representations**

The activation of frontal motor-related systems also relates to the process by which internal representations of the limb are updated to include a prosthesis in the motor plan. Several studies demonstrate that intact subjects possess the ability to incorporate tools into the internal representation of their limbs on morphological (Cardinali et al. 2009), behavioral (Gentilucci et al. 2004) and perceptual levels (Farne et al. 2005; Cardinali et al. 2009). An important question related to this work is how an external object such as a novel prosthetic device could be incorporated into the body schema of an intact subject or person with amputation. Previous neurophysiological studies have documented the ability of macaques to incorporate tools into their internal body representations. In one particular study, upon training with two sets of pliers, cortical neurons that were involved in control of finger grasp were also activated by the use of the pliers to grasp (Umiltà et al. 2008). The implication being that the pliers had become incorporated into the body schema and now relied upon F5 premotor cortical areas shared with control of the hand. An fMRI study in humans also showed end-effector independent activity in the anterior intraparietal-ventral premotor area (a suggested homologue for F5 in macaques) (Jacobs et al. 2010). Specifically, subjects showed comparable activation in this area (among other motor related areas) upon planning grasping tasks with their own hand and with a grasping tool. The suggestion was made that limb representations had been updated to include the use of the tool in a functionally relevant manner.

Given this background, the results of the dissertation suggest that prostheses may be generally perceived as tools and can likewise be incorporated into the body schema. Indeed, recent work in novel force field motor adaptation suggests that persons with

unilateral amputation are capable of incorporating prostheses into their body schema during goal oriented reaching tasks to the extent that performance with their prosthetic limb is comparable to that of their own intact limb (Metzger et al. 2010) and to unimpaired individuals (Schabowsky et al. 2008). Further, this dissertation supports the notion that the process of incorporating the prosthetic device into the body schema is more effective with exposure to limb matched imitation training. Once a prosthetic device is incorporated, observing a matching prosthetic device triggers mechanisms of motor resonance and results in greater engagement of the parietofrontal system. This notion is further supported by the beneficial behavioral effects of matched limb imitation in both persons with limb amputation using their prosthesis and in intact users of the FAMS.

## **Future Motor Control Studies**

### **Learning and Adaptation**

This dissertation also has important implications on motor adaptation and learning, as the parietofrontal system has been shown to be important for both of these processes. In a recent study by Buch et al. (2012), parietofrontal integrity in stroke survivors was directly correlated to their ability to learn new motor imagery skills. The authors stated that connectivity between the parietal and frontal regions along the superior longitudinal fascicles directly facilitated the acquisition of new motor skills and that deficits in adaptation during a training paradigm were found in subjects exhibiting damage to these pathways (Buch et al. 2012). Enhancing the engagement of the parietofrontal network in prosthesis users may increase their ability to adapt to the novel constraints of their new limb state and to learn new skills using the prosthesis. Future

work should investigate these processes using longitudinal motor learning paradigms with matched limb imitation training.

Recent work by Schabowsky et al. could be replicated and combined with the methods presented in this dissertation (Schabowsky et al. 2008). In that study, persons with transradial amputations used their prosthetic devices to interact with a robotic manipulandum in a horizontal plane reaching task. As subjects reached towards targets, forces were exerted via the robot to impart initially large movement errors. Subjects then adapted to the presence of such force field disturbances to maintain straight reaching trajectories. The decrease in movement errors was used to quantify motor adaptation. Results of the study showed that early learning rates were comparable to those of intact subjects, but in the late learning phase, prosthesis users exhibited higher movement error magnitude and variability.

One extension of this work would be to place persons with acute upper extremity amputations and naïve FAMS users in a similar motor learning paradigm after being trained on their new device with either matched or mismatched limb imitation. Both the training sessions and robotic force field experiments could be repeated over a longitudinal paradigm to investigate short and long term effects of action observation training on novel prosthesis use and motor learning. One hypothesis would be that, due to the enhanced engagement of the parietofrontal network, subjects trained with matched limb imitation would demonstrate lower movement error and variability than their counterparts trained with mismatched limb imitation. This hypothesis and approach are reasonable based on the results presented in this dissertation.

## **Body Schema**

In the preceding chapters, the concept of incorporating a prosthetic device into the cortical representation of the limbs, or body schema, has been discussed extensively. This aspect of the motor system can be indirectly studied by the investigation of peri-personal space; the area around the body in which visual and tactile sensory input coincide. In other words, this is the space that we can both see and touch with our hands. The neural substrates for such a phenomenon are multisensory processing neurons that respond to visual and tactile stimulation (Bremmer et al. 2001). A study by Farne et al. demonstrated that this peri-personal space can be extended by the use of an elongated tool (Farne et al. 2005). The authors stated that the shape and direction of this extension is determined by the length of the tool and the location of the functional end along that length.

A viable extension of this work is to investigate peri-personal space in prosthesis users, and to use this metric as a tool for measuring the degree to which a prosthesis is incorporated into the body plan. Ideally, this proposed study would be performed immediately after a unilateral upper extremity amputation. During this experiment, the peri-personal space of the intact arm could be quantified, in addition to the peri-personal space of the newly shortened residual limb. The next data collections would take place immediately after the initial fitting of a prosthesis, and at several time intervals later. This approach would allow for the quantification of the peri-personal space as a function of practice.

Further, the longitudinal training paradigm presented in Chapter 7 could be adapted for this proposed study in order to investigate the longitudinal effects of matched versus mismatched limb imitation on prosthesis user peri-personal space. A more practical augmentation of this experiment would be to study the peri-personal space of



intact subjects before donning the FAMS, immediately after donning the FAMS, and after training with the FAMS. A reasonable hypothesis in either case is that prosthesis users trained with matched limb imitation would exhibit a greater extension of their peri-personal space and thus, provide support for the more complete incorporation of the prosthesis into their body schema. This result would speak to the subject's perception of their reachable space and may provide insight into both the incorporation of the device and the related functional benefits.

### **Perspective**

An interesting question raised by this dissertation involves the perspective in which motor task demonstration videos are presented to the subjects. All of the videos reported in the previous chapters were recorded with the actor in the sagittal plane. It is an open question as to which angle is most appropriate in this type of video training and there are several options for investigation. An egocentric perspective would closely model that which a subject observes as they perform a task themselves. Contrastingly, an allocentric perspective is most like the viewpoint experienced as a subject observes another agent, such as their occupational therapist. It is also possible that a combination of these perspectives would yield the most beneficial results.

There is a rich body of literature dealing with the concept of action perception given presentation perspectives. A recent study by Kelly and Wheaton recruited subjects to judge the functional outcomes of various tool-use actions presented in both egocentric and allocentric perspectives (Kelly and Wheaton 2013). Subjects judging the outcome of actions presented in the egocentric perspective showed both higher accuracy and lower

latency compared to actions presented in the allocentric perspective. The authors suggest that the egocentric perspective better facilitates action perception as it can be understood from their own internal perspective. Activation in the left parietal lobe is thought to underlie such resonance with the cortical representation of the body (Iacoboni et al. 1999). Contrastingly, the allocentric perspective requires an additional visuomotor transformation to permit action understanding, as has been shown by increased activity in the right posterior parietal cortex (Watanabe et al. 2011).

There are potential parallels between this work in perspective and the concepts presented in the dissertation. Both topics involve the relative contributions of two action encoding systems whose activity is influenced by motor resonance (left parietofrontal) and visuomotor complexity (right occipitoparietal). Synthesizing these two bodies of work may yield useful insights into action-observation therapy. A potential future study would involve expanding the work of Chapter 7 to include matched limb imitation from both the egocentric and allocentric perspectives. A reasonable hypothesis would be that matched limb imitation presented from the egocentric perspective would yield greater engagement of the parietofrontal network and reduced movement variability compared to that of allocentric perspective. In this scenario, the imitation task complexity would be reduced even further, as the presentation perspective is matched to that of subjects' internal reference frame in addition to matching the observed limb type.

## **Future Clinical Applications**

### **Use of the FAMS**

There are several findings of this dissertation that have rehabilitation implications and warrant further investigation in a clinical setting. First, this work provides strong

evidence for the validity of using the FAMS in the development of prosthesis training protocols. While devices comparable to the FAMS have been previously used in intact subjects to investigate prosthesis control (Bouwsema et al. 2010a) and functionality (Bouwsema et al. 2008; Smurr et al. 2008), this is the first instance of using such a device to research basic neuroscience and rehabilitation methods. Substantial support for this methodology is provided in Chapter 7 by the differential longitudinal engagement of the parietofrontal and parietooccipital cortical action encoding networks in intact users of the FAMS. This effect of matched vs. mismatched limb imitation is also seen in persons with amputation in Chapter 4.

Thus, use of the FAMS appears to be a viable strategy for developing action observation therapy protocols for training with a prosthetic device. The use of the FAMS in intact subjects provides a number of significant advantages, including the ability to more precisely control for factors such as original handedness, side and level of amputation, time since amputation, and daily use of a prosthetic device. Additionally, due to the ease of recruiting intact subjects, experimental paradigms can be fine-tuned prior to enrolling persons with amputations into a larger longitudinal study.

### **Developing Novel Rehabilitation Protocols**

This work presents the first evidence suggesting that persons with limb amputation training to use their novel prosthetic device may benefit from action-observation therapy that provides the opportunity to observe and imitate actions performed by other prosthesis users. Important questions to ask at this point include: “How could these results translate to clinical benefits?” and “How could these results contribute to the problem of prosthesis abandonment?”

First, it should be noted that the movements used in this dissertation were intentionally simplified in order to be incorporated into a series of controllable experiments. Namely, the block rotation task was chosen as it featured rotational and translational movement components that were obstructed or modified while using the FAMS. While these movements are somewhat basic, we are proposing that improvements in performance at this level may also be beneficial to more complex tasks that require the combination of such simple movements. For example, improving the process by which a fundamental movement such as end-effector rotation is learned may yield behavioral benefits when applying that skill towards the turning of a door knob.

In a 2007 review of upper extremity prosthesis use, Biddiss and Chau reported that persons with amputation abandoned their devices for a number of reasons including poor training, limited usefulness, and poor initial prosthetic experience. We are proposing that the matched limb training methods presented in this dissertation may alleviate some of these difficulties by enhancing the initial rehabilitation experience and the formation of fundamental movement skills. Thus, it is the hope that by reducing these early challenges, patients will be less likely to abandon their devices.

In order to expand the neuroscience foundation of this work and to elaborate on potential clinical benefits, additional work is suggested. Given the dissertation results, further expansion of the experimental paradigm into a larger population of persons with upper extremity amputation is warranted. There is precedence in the literature for applying action observation therapy as a strategy to rehabilitate motor deficits.

An article by Ertlet et al. describes one such study involving motor rehabilitation in stroke survivors (Ertelt et al. 2007). Subjects in that study participated in either action

observation with concomitant physical practice or physical practice alone; both over a treatment period of four weeks. Treatment in the action observation group included repetitive focused observation of video demonstrations of ADLs involving the arm and hand. Subjects were then instructed to perform the observed actions with their paretic hand. Training sessions were monitored by physical therapists that guided subject activity and ensured compliance. The control group participated in an identical protocol with the exception that video sequences contained only abstract shapes instead of ADL demonstrations (Ertelt et al. 2007).

Both groups demonstrated motor function improvements compared to their own pre-treatment baseline, and the action observation group exhibited more improved motor functions compared to the control group. Motor function was quantified using the Frenchay Arm Test, Wolf Motor Function Test, and Stroke Impact Test. Improvement in the experimental group was maintained after an eight-week follow-up. Brain imaging using fMRI was also performed in this study and results in the experimental group showed greater activation in the bilateral ventral premotor cortex, bilateral superior temporal gyrus, and the supplementary motor area; all regions implicated in the parietofrontal action encoding network (Ertelt et al. 2007).

There are parallels between the results of this study and those of the dissertation, as both populations showed greater engagement of the parietofrontal action encoding network and enhanced motor performance after participating in action observation training. Extending these findings by implementing a longitudinal action observation study in persons with limb amputation would be a worthwhile endeavor. Such a study could include at least two branches comparing the cortical and behavioral outcomes of

matched limb action observation paired with physical practice versus traditional physical practice accompanied with an occupational therapist. This would not only expand the questions posed in the dissertation, but would also compare the results to those of standard rehabilitation methods.

It should be noted that creating a matched limb condition can be accomplished in several ways. One strategy would involve the recruitment of persons with upper extremity amputation who are expert users of their prostheses. These individuals could provide useful insight into device operation and their limb states would most closely match that of the prosthesis trainees. Intact occupational therapist may also provide limb matched demonstrations by donning the FAMS themselves prior to demonstrating a particular clinical activity. This strategy would prove more practical to implement, as clinicians would require only a FAMS device and not access to expert prosthesis users. Additionally, occupational therapists will be best equipped with knowledge regarding the most effective rehabilitative concepts and methodologies. However, the degree to which the capabilities and kinematics of the FAMS user match those of the prosthesis trainee will vary.

A potentially useful supplement to standard occupational therapy could also involve focused observation of matched limb video demonstrations similar to those presented in this dissertation. Finally, virtual reality modules could be developed to create interactive matched limb imitation experiences. An advantage of these last two applications is that they could theoretically be implemented at home and thus could provide additional rehabilitation without requiring the additional expenditure of clinical hours, equipment, or resources. These technologies could also tap into the burgeoning

field of telemedicine and provide clinicians with supplementary clinical data for managing their patients' care.

## APPENDIX A

### TRINITY AMPUTATION AND PROSTHESIS EXPERIENCE

#### SCALES (TAPES)

PLEASE RESPOND TO THE QUESTIONS BELOW

**FOR THE DEVICE YOU WERE USING DURING THE EXPERIMENT**

**ANSWER AS YOU WOULD HAVE NEAR THE TIME OF THE EXPERIMENT (XX/XX/20XX)**

- |   |                      |             |
|---|----------------------|-------------|
| A) What is the power source for the device?       | Body-powered harness | Myoelectric |
| B) What is the terminal device?                   | Hook                 | Hand        |
| C) How many hours per day do you use your device? | _____ hrs /day       |             |

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
1) I have adjusted to having an artificial limb..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
2) As time goes by, I accept my artificial limb more..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
3) I feel that I have dealt successfully with this trauma in my life..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
4) Although I have an artificial limb, my life is full..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
5) I have gotten used to wearing an artificial limb..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
6) I don't care if somebody looks at my artificial limb..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
7) I find it easy to talk about my artificial limb..... [ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
8) I don't mind people asking about my artificial limb.. .....[ 1 ]	[ 2 ]	[ 3 ]	[ 4 ]	[ 5 ]	
9) I have a difficulty in talking about my limb loss in conversation..... [ 5 ]	[ 4 ]	[ 3 ]	[ 2 ]	[ 1 ]	
11) An artificial limb interferes with the <u>ability</u> to do my work..... [ 5 ]	[ 4 ]	[ 3 ]	[ 2 ]	[ 1 ]	
12) Having an artificial limb makes me more dependent on others than I would like to be..... [ 5 ]	[ 4 ]	[ 3 ]	[ 2 ]	[ 1 ]	
13) Having an artificial limb limits the <u>kind</u> of work that I can do..... [ 5 ]	[ 4 ]	[ 3 ]	[ 2 ]	[ 1 ]	
14) Being an amputee means that I can't do what I want to do..... [ 5 ]	[ 4 ]	[ 3 ]	[ 2 ]	[ 1 ]	
15) Having an artificial limb limits the <u>amount</u> of work I can do..... [ 5 ]	[ 4 ]	[ 3 ]	[ 2 ]	[ 1 ]	



## APPENDIX B

### MINNESOTA MANUAL DEXTERITY TEST (MMDT)

*Evaluation instructions for each group on training days 2,3,4 (Aim 3):*

A) Place game board centered in front of subject, elbow in cushion, align pink row with wrist crease

B) Practice session = moving green cylinders 1 and 2 from the left holes to the right holes.

C) Game sessions:

- 1) Arm begins in home base
- 2) Start stop watch and tell subject to begin, "Perform task as quickly and accurately as possible."
- 3) Move each numbered cylinder from its number-matched hole on left to number-matched hole on right, in order 1-8
- 4) Move each numbered cylinder from its number-matched hole on right to number-matched hole on left, in order 1-8
- 5) Arm goes back to home base
- 6) Stop stop watch, record time
- 7) Repeat 3 times

D) Game rules:

- 1) Must follow instructions correctly, start over if error made
- 2) Cylinders must land flat in holes. If not, subject must fix them
- 3) If cylinder is dropped, subject must pick it up and continue (if cylinder falls over on side and/or rolls, experimenter rights it in place)



## **APPENDIX C**

### **PANTOMIME RECOGNITION SCALE (PRS)**

#### ***Evaluation instructions for pantomime movements***

- 1      Movement is present, but difficult to decipher and prolonged with pauses.
- 2      Movement is recognizable, but with severe temporal and spatial errors.
- 3      Movement is fair, but with moderately prolonged movement sequences and temporal, spatial, and/or context errors.
- 4      Movement is error free.

## APPENDIX D

### EDINBURGH HANDEDNESS INVENTORY

Please indicate with a check (✓) your preference in using your left or right hand in the following tasks.

Where the preference is so strong you would never use the other hand, unless absolutely forced to, put two checks (✓✓).

If you are indifferent, put one check in each column (✓ | ✓).

Some of the activities require both hands. In these cases, the part of the task or object for which hand preference is wanted is indicated in parentheses.

Task / Object	Left Hand	Right Hand
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking a Match (match)		
10. Opening a Box (lid)		
Total checks:	LH =	RH =
Cumulative Total	CT = LH + RH =	
Difference	D = RH – LH =	
Result	R = (D / CT) × 100 =	
Interpretation: (Left Handed: R < -40) (Ambidextrous: -40 ≤ R ≤ +40) (Right Handed: R > +40)		

<sup>1</sup> Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9, 97-113.

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## **VITA**

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